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USSR Report

LIFE SCIENCES

BIOMEDICAL AND BEHAVIORAL SCIENCES

(FOUO 16/81)



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BIOTECHNOLOGY

UDC 612.172.4---72(083.74)

ELECTROCARDIOGRAPHIC INSTRUMENTS: BASIC TECHNICAL SPECIFICATIONS--GOST 19687-74

Moscow ELEKTROKARDIOGRAFIY: OBSHCHIYE TEKHNICHESKIYE USLOVIYA (GOST 19687-74)
in Russian 1974 (signed to press 10 Jun 74) pp 1-18

[All-Union State Standard, Group R24, L. A. Burmistrov, editor]

[Text] Decree of the State Committee for Standards of USSR Council of Ministers,
9 April 1974, No 847, period of validity set: from 1 January 1975 to 1 January
1978

Nonobservance of the standard will be prosecuted by law.

The instant standard affects electrocardiographs (hereinafter EKG's) designed for
diagnostics in therapeutic and prophylactic medical institutions.

1. Technical Requirements

1.1 With respect to accuracy of signal form reproduction and recording of
amplitudes and time intervals, EKG's of three classes--1, 2 and 3--must be
manufactured.

1.2 With respect to the number of channels, the following types of EKG's must be
manufactured:

- single-channel;
- two-channel;
- four-channel;
- six-channel.

In technically valid cases it is acceptable to manufacture three-channel EKG's.

1.3 With respect to the type of recording element and sort of recording medium,
the following kinds of EKG's must be manufactured:

- pen EKG's recording with ink on paper;
- pen EKG's recording on thermosensitive paper;
- pen EKG's recording on paper and using a recorder chart;
- pen EKG's recording on an electrosensitive chart;
- jet EKG's recording on paper;
- beam-type EKG's recording on photographic paper or film with subsequent
development;
- beam-type EKG's recording on paper with immediate development;
- beam-type EKG's recording on semiconductive paper;

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beam-type EKG's recording on paper.

- 1.4 With respect to the type of power pack, EKG's must be manufactured:
 - with a feed line;
 - with an autonomous power supply;
 - with a composite power supply;

Note: At the purchaser's request, the EKG's must be fed from an alternating current supply-line at a frequency of 50 and 60 Hz.

- 1.5 The standard labeling of the EKG's is governed by GOST 17562-72
- 1.6 The basic parameters of the EKG's must correspond to those presented in table 1.
- 1.7 The potential lead points and the electrocardiographic leads of the EKG's must have the labels presented in appendix 1.
- 1.8 The EKG must provide electrocardiogram recording at the leads the labelings of which are indicated in appendix 1.
- 1.9 The external edges of the electroconductive part of the electrode for leading potentials from the thorax which interface with the skin, must form a circle of no more than 20 mm in diameter.
- 1.10 The EKG's must provide recording of processes in an orthogonal system of coordinates.
- 1.11 The input circuits of the EKG's must be assembled in such a manner that connecting the source of constant voltage between the wires of the lead cable in the polarity indicated in table 2, produces a positive (upwards) deviation of the recording line.
- 1.12 The labeling of the lead cable is presented in fig 1.
- 1.13. The technical documentation approved by the established procedure for EKG's of the specific types, shall also contain the following additional requirements:
 - for electrical safety;
 - for resistance to climatic and mechanical influences;
 - for the time to establish operating conditions;
 - for the input and output parameters for connecting accessories or gages;
 - for the power line parameters;
 - for labeling and commutating leads;
 - for the parameters of the battery volume indicator;
 - for the accuracy of limb potential neutralization when the midpoints of single-band leads are obtained;
 - for the calibrator;
 - for electrical power used;
 - for overall dimensions;
 - for mass.

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Table 1.

(2) Наименования параметров		(1) Нормы для классов точности		
		1	2	3
(3)	1. Диапазон измерения напряжения U , мВ	0.03-5	0.03-4	
(4)1	2. Диапазон измерения интервалов времени τ , с	0.01-2.00		
(5)	3. Погрешность измерения напряжения ΔU , мВ	$\pm \left(\frac{0.1}{U} + 0.06U \right) \left \pm \left(\frac{0.15}{U} + 0.1U \right) \right \pm \left(\frac{0.2}{U} + 0.15U \right)$		
(6)	4. Погрешность измерения интервалов времени $\Delta \tau$, с	$\pm \left(\frac{0.5}{v} + 0.05\tau \right)$		$\pm \left(\frac{0.5}{v} + 0.1\tau \right)$
(7)	5. Чувствительность ξ , мм/мВ	минимальная	5	
		средняя	10	
		максимальная	20	
(8)	6. Скорость движения носителя записи v , мм/с	1; 2,5; 5; 10; 25; 50; 100; 250	25 50 100	25 50
(9)	7. Эффективная ширина записи канала E , мм, не менее	100	40	
(10)	8. Пределы смещения нулевой линии от среднего положения k , мм	± 40	± 15	
(11)	9. Выброс на переходной характеристике δ , %, не более	5	10	
(12)	10. Коэффициент относительной несимметрии $K_{\text{он}}$, не более	$1 \cdot 10^{-2}$		
(13)	11. Эквивалентное сопротивление синфазных помех $R_{\text{сф}}$, Ом, не более	15	100	
(14)	12. Коэффициент взаимовлияния между каналами W , %, не более	2		
(15)	13. Максимальная несинхронность регистрации между каналами, мм, не более	0.4		
(16)	14. Толщина линии записи, мм	0.3-1		
(17)	15. Скорость дрейфа нулевой линии, приведенная ко входу $v_{\text{др}}$, мВ/с, не более	30	50	
(18)	16. Уровень внутренних шумов, приведенный ко входу $U_{\text{ш}}$, мВ, не более	10	20	30
(19)	17. Гистерезис записи λ , мм, не более	1	1,2	
(20)	18. Время успокоения, с, не более	3		

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(2) Наименования параметров	(1) Нормы для классов точности		
	1	2	3
(21) 19. Скорость записи u_3 , м/с, не менее	10	1	
(22) 20. Неравномерность амплитудно-частотной характеристики α , %	± 5	± 10	± 15
(23) 21. Верхняя граничная частота f , Гц	От 800 до 1000	От 70 до 100	От 60 до 70
(24) 22. Завал вершины переходной характеристики за время 2,2 с σ , %, не более	60		

Key:

1. Norms for classes of accuracy
2. Parameters
3. Range of voltage measurement, U , in mV
4. Range of time interval measurement, U , in mV
5. Accuracy of voltage measurement, ΔU , in mV
6. Accuracy of time interval measurements, Δt , in seconds
7. Sensitivity, ξ , in mm/mV
 - Minimum
 - Average
 - Maximum
8. Rate of movement of recording medium, h , in mm/s
9. Effective recording width of channel, E , in mm, no less than
10. Range of bias of zero line from median position, h , in mm
11. Rejection on transient response δ , in percent, no greater than
12. Coefficient of relative asymmetry, K_{ra} , no greater than
13. Equivalent resistance to inphase interference, $R_{e(1)}$, no greater than
14. Coefficient of interference between channels, W , in percent, no greater than
15. Maximum asynchronicity of recording between channels, in mm, no greater than
16. Thickness of recording line, mm
17. Drift rate of zero line attributed to input, v_{dr} , $\mu V/s$, no more than
18. Level of internal noise attributed to input, U_n , μV , no more than
19. Recording hysteresis, λ , mm, no greater than
20. Damping time, s, no greater than
21. Recording rate, v_3 , m/s, no less than
22. Irregularity of amplitude-frequency characteristic, α , in percent
23. Upper edge frequency, f , in Hz
24. Drop in peak of transient response in 2.2 s, σ , in percent, no greater than

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Notes:

1. EKG's intended for operation in automatic systems for analysis and processing of electrocardiograms, may have an effective recording width of 30 mm.
2. In place of the coefficient of relative asymmetry and equivalent resistance to inphase interference, it is permissible to use as the standard the rejection coefficient (K_R), the value of which must be no less than 60 dB for EKG's of all classes.
3. Single-channel EKG's may have a rate of recording medium movement equal to 25 and 50 mm/s.
4. EKG's of the first class of accuracy with jet-on-paper recording may have a rate of recording medium movement equal to 5, 10, 25, 50 and 100 mm/s.
5. EKG's of the first class of accuracy must offer the possibility of limiting the upper edge frequency to 65-75 Hz and to 250-300 Hz.
6. The dispersion of the rated values of resistances forming a unipolar lead must not exceed 2 percent for EKG's of the first class, 3 percent for the second class and 4 percent for the third class.

Table 2.

Polarity of Voltage in Wires of Lead Cable	Lead Marking						
	<u>I</u>	<u>II</u>	<u>III</u>	<u>aVR</u>	<u>aVL</u>	<u>aVF</u>	<u>V₁-V₆</u>
Minus	R	R	L	L F	F R	R L	R L F
Plus	L	F	F	R	L	F	C ₁ -C ₆

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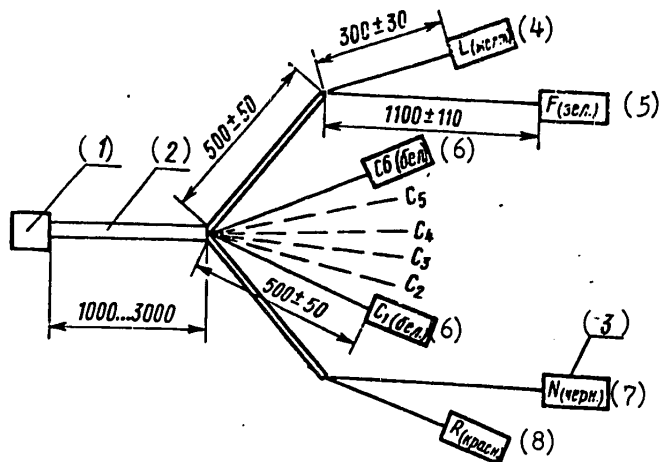


Figure 1.

Key:

- | | |
|---|-----------|
| 1. Connector for connecting cable to EKG or site of cable lead to EKG | 4. Yellow |
| 2. Common cord | 5. Green |
| 3. Device for connecting wire to electrode | 6. White |
| | 7. Black |
| | 8. Red |

Note: The number of wires in the lead cable for connection to the thoracic electrodes must be equal to the number of thoracic electrodes employed simultaneously or consecutively according to the commutation of the EKG leads. If the EKG is designed for use of one thoracic electrode only, the wire for connecting to this electrode must be marked with the letter S.

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1.14 The probability of reliable operation of the EKG's for 500 hours of relatively uninterrupted operation with confidence of $P^*=0.8$ shall be no less than 0.8.

2. Inspection Rules

2.1 In order to test the compliance of the EKG's with the requirements of the instant standard, the manufacturing enterprise must conduct state, acceptance, periodical and standard tests.

2.2 State testing of EKG's is governed by GOST 8.001--72.

2.3 Each EKG is subjected to acceptance testing for compliance with the requirements of pars 1-22, table 1; 1.12; 1.14 (except for testing for resistance to climatic and mechanical influences).

2.4 EKG's from among those which passed acceptance testing are subjected to periodical testing. Periodical testing is conducted once annually on three EKG's for compliance with all requirements of the instant standard except for par. 1.14, and once every three years on eight EKG's for compliance to par 1.14. If during periodical testing the noncompliance of an EKG with at least one of the requirements of the instant standard is established, the test results are considered unsatisfactory, and repeat testing of a doubled number of test specimens for the complete program must be performed. The results of repeat testing are conclusive.

2.5 When the model, design, materials or industrial manufacturing process is changed, standard testing of EKG's is performed on three EKG's for compliance with all requirements of the instant standard, except for compliance with par. 1.14, and on eight EKG's for compliance with the requirements of par. 1.14. If during standard testing for compliance with all requirements of the instant standard except for par 1.14, the EKG's do not meet at least one of the requirements, repeat tests are conducted on a doubled number for the complete program.

3. Methods of Testing

3.1 The basic parameters of the EKG's are tested using a source of a signal of subsonic and low frequencies having an output signal in the form of a sinusoid and a sequence of orthogonal pulses and separate serrate pulses. Measurement on the recording is performed using rulers with a scale division of 0.5 mm. Measurement of dimensions of less than 15 mm is performed using rulers with a scale division of no less than 0.1 mm. No allowance is made for the width of the recording line (fig 2).

3.2 The test signal to the input of the EKG channel is fed through the lead cable at any of the electrocardiographic leads which may be commutated to a given channel. As this takes place, the value of the mean level of constant voltage of any polarity between each of the pairs of active electrodes and the neutral electrode must be no less than 100 mV, and between the active electrodes--not less than 50 mV.

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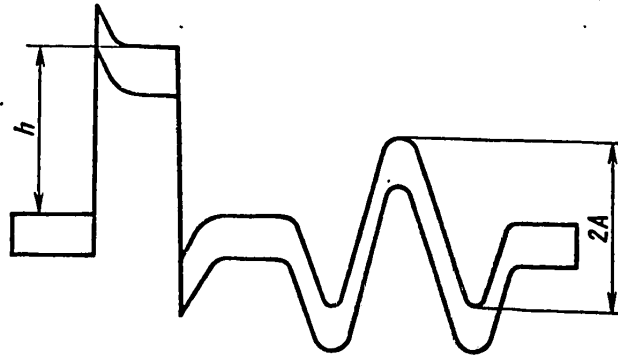


Figure 2.

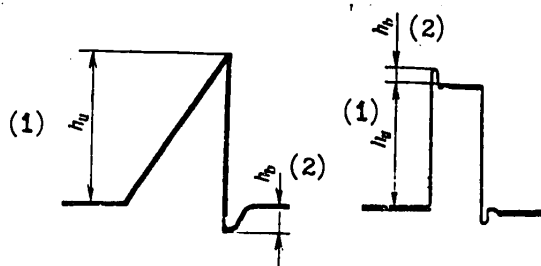


Figure 3.

Key:

1. h_1
2. h_v

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3.3 The basic parameters of the EKG's are tested after test voltages with a line frequency-inphase value of $2 \pm 0.2 V_{eff}$ and an antiphase value of $2 \pm 0.2 mV_{eff}$ are first fed simultaneously to the inputs of the channels for three s.

3.4 The measurement and error ranges of the EKG's (par. 1-4, table 1) are tested under the influence of extreme values of influential factors indicated in the technical documentation.

3.5 The compliance of the EKG's with the requirements of pars 1.2; 1.3; 1.5; 1.7-1.10; 1.12; 4.1-4.6 is tested by external inspection and a measuring instrument which offers the required accuracy.

3.6 The accuracy of electrocardiogram recording (par. 1.8), as well as of the input circuits wiring (par. 1.11), is tested at average sensitivity at the electrocardiographic leads listed in appendix 1 by recording an orthogonal pulse with an amplitude of $1 \pm 0.1 mV$. The depiction of the impulse must be positive for each of the leads on all channels to which this lead may be commutated.

3.7 Error in voltage measurement (par 3, table 1) is determined by connecting to the EKG input the maximum values of the equivalents of electrode full resistance to the electrical equivalent of the subject presented in appendix 2 and recording serrate or orthogonal test pulses of positive and negative polarity in accordance with table 2, at nominal sensitivity values (par 5, table 1) and at any location of the zero line, h (par 8, table 1), within the range of the effective recording width of the channel, E, (par 7, table 1) based on the correlation:

$$\pm U_t \leq \frac{E}{2} \pm |h| \quad \text{where } h \leq 0;$$

$$\pm U_t \leq \frac{E}{2} \pm |h| \quad \text{where } h \geq 0.$$

Pulse Amplitude mV	Pulse Width s
5.00	0.015
4.00	0.015
2.00	0.010
1.00	0.100
0.40	0.150
0.20	0.200
0.10	0.100
0.03	0.100

Error in determining the amplitude of the test pulse must not exceed one-third of the acceptable error in voltage measurement for the accuracy class of the EKG's being tested. Error in determining pulse width must not exceed ± 2 percent. The build-up time of the orthogonal test pulse must be no greater than 0.1 ms.

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The period of the orthogonal pulse sequence must be no less than 1 s.

When the requirements of par. 3, table 1 are met, the requirements of pp 1; 5; 7-9, table 1 are considered to have been met.

Amplitudes h_1 and h_v are measured on the recording (fig 3).

Error in voltage measurement (par 3, table 1) is determined in mV according to the formula:

$$\Delta U = U - \frac{h_1}{k}$$

Error in voltage measurement is determined in three ways: by the lapse of time to establish operating conditions; 2 hours after turning on the power; 4 hours after turning on the power.

Rejection on the transient response (par 9, table 1) is determined according to the formula:

$$\delta = \frac{h_v}{h_1} \cdot 100 \text{ percent}$$

Note. Up to 1977, the method of testing by serrate pulses is optional.

3.8 Error in measurement of time intervals (par 4, table 1) is determined at all the values of the rate of movement of the recording medium, v , stipulated in par 6, table 1, by recording a sinusoidal or orthogonal-shaped periodic signal with a period of $T = \frac{1}{v}$ s fed to the input of the EKG's for 5 s. Error in determining period duration must not exceed one-third of the acceptable error of measurement of time intervals depending on the accuracy class of the EKG's being tested.

When the requirements of par 4, table 1 are met, the requirements of pars 2 and 6, table 1 are considered to have been met.

The time intervals t in the range specified in par 2, table 1 are determined by the number of periods n of the test signal

$$t = n \cdot T$$

The time intervals on the recording, t (fig 4), which correspond to the time intervals t , are determined by measurement of the length l , in mm, of any segment of the recording containing n periods of the test signal with allowance for the relation $0.5 \leq l \leq 50$, and by computing

$$t_s = \frac{l}{v}$$

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Figure 4.

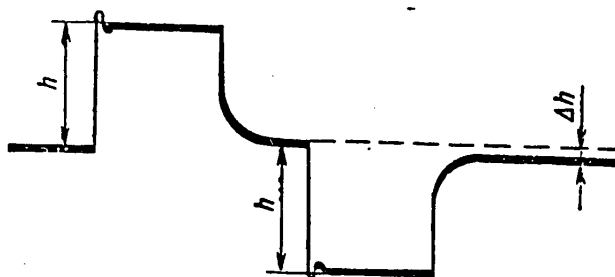


Figure 5.

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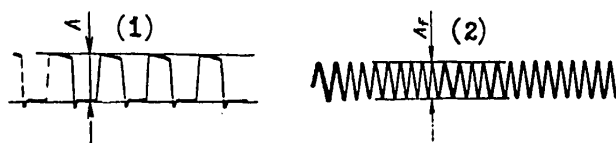


Figure 6.

- Key:
1. A
 2. A_f

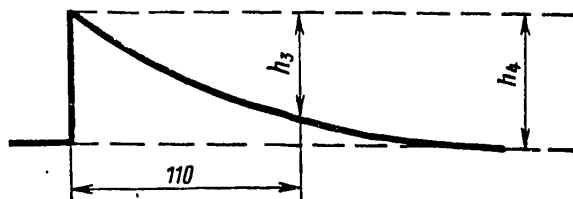


Figure 7.

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Error in measurement of time intervals $\Delta\tau$ is determined according to the formula:

$$\Delta\tau = \tau - \tau_s.$$

3.9 The coefficient of relative asymmetry (par 10, table 1) is determined at all possible combinations of the equivalents of electrode full resistance in accordance with appendix 2 by recording a sequence of inphase orthogonal test pulses fed to the input of the EKG's at any sensitivity. The width of the pulses in the sequence is 0.2 ± 0.02 s. The on-off time is 2. The amplitude of the pulses must be within the linearity range of the amplitude characteristic of the EKG's for the inphase signal.

The amplitude of impulses, A, is measured in mm on the recording, with allowance for rejection.

The coefficient of relative asymmetry is determined according to the formula:

$$K_{ra} = \frac{A}{U \cdot \xi}.$$

3.10 Equivalent resistance to inphase interference (par 11, table 1) is determined at maximum unbalances of the input circuits by recording a sinusoidal signal at a frequency of 50 ± 2 Hz with voltage of U_p (appendix 2).

The double amplitude of the sinusoid A is measured on the recording.

Equivalent resistance to inphase interference is determined according to the formula:

$$R_{e(1)} = \frac{A \cdot 10^3}{2\sqrt{2} \xi \cdot U_{p}},$$

where A is the double amplitude of the sinusoid measured on the recording, in mm;
 ξ is the sensitivity of the EKG's, in mm/mV;
 U_p is the voltage fed to the input of the EKG's in conformance with appendix 2, V_{eff} .

3.11 The coefficient of interference between channels (par 12, table 1) is determined by recording a sequence of orthogonal test pulses fed to the input of one of the channels of the EKG while the inputs of the other channels are closed. The width of the pulses in the sequence is 0.2 ± 0.02 . The on-off time is 2. The sensitivity of the channel on which the test signal is fed must be minimum, and the intensity of the input signal, such as to ensure recording, the double amplitude of which is equal to the effective recording width of the channel. The sensitivity of channels with closed inputs must be maximum, and the amplitude-frequency characteristic must not be restricted at the top.

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The test signal is fed in turn to all channels of the EKG.

Pulse amplitude, A, is measured in mm on a recording of the channels with closed inputs with allowance made for rejection.

The coefficient of interference between channels is determined according to the formula:

$$W = \frac{A}{E} \cdot 100 \text{ percent.}$$

3.12 The maximum asynchronism of recording between channels (par 13, table 1) is determined by recording a discontinuity in constant voltage fed to all inputs simultaneously. The build-up time of the test voltage must be no greater than 0.4 ms.

The maximum deviation along the time axis for two channels between inphase points in the process is measured on the recording.

The requirement of par 13, table 1 must be met at any position of the zero line of the channel.

3.13 The thickness of the recording line (par 14, table 1) is determined by recording the zero line with the channel input closed and at minimum sensitivity.

3.14 The drift rate of the zero line (par 15, table 1) and the level of internal noise (par 16, table 1) attributed to an input are determined at the maximum sensitivity of the EKG by recording the zero line for 5 s. The maximum values of equivalents of the electrode impedances of the electric equivalent of the subject are connected to the input of the EKG (appendix 2).

The size of the monotonic vertical displacement of the zero line caused by amplifier drift, h_{dr} , and the width of the noise track, h_n (defined as exceeding the width of the zero line without making allowance for individual rejections) are measured in mm on the recording.

The drift rate of the zero line attributed to an input is determined according to the formula:

$$V_{dr} = \frac{10^3 \cdot h_{dr}}{t \cdot t}$$

where t is the time in which the drift of the zero line is measured, in seconds.

The level of internal noise attributed to an input is determined using the formula:

$$U_n = \frac{10^3 \cdot h_n}{t}$$

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3.15 Recording hysteresis (par 17, table 1) is determined at maximum sensitivity by recording orthogonal pulses of first positive, and then negative, polarity at a rate of movement of the recording medium equal to 50 mm/sec at any position of the zero line. The input to which the test pulses are fed and a diagram of their feeding must be indicated in the technical documentation for EKG's of the specific type.

The height of the fronts of test pulses on the recording, h , must be no less than 10 mm, the duration of pulse decay, no less than 20 μ s. The interval between pulses must be from 0.2 to 0.4 seconds.

Values h and Δh are measured on the recording (fig 5).

3.16 The damping time (par 18, table 1) is determined at all values of sensitivity of the EKG specified in par 5, table 1 by feeding to its input a discontinuity in constant voltage with an amplitude of 50 ± 5 mV. No later than 3 seconds after feeding the voltage, the "damping" knob must be pressed. The zero line must be set in the initial stable position which preceded the feeding of the discontinuity in constant voltage with error not exceeding 2 mm for a duration of not more than 3 seconds, including the time the knob is pressed.

The damping time, which corresponds to the length of time the knob is pressed during which the zero line is set in the initial position, is measured on the recording by the length of zero line segments. Damping time is determined by test voltage of both polarities.

3.17 Recording speed (par 19, table 1) is determined by recording a sinusoidal signal with double amplitude h and frequency f .

The maximum recording speed $v_{z.max}$ is determined according to the formula:

$$v_z = \pi \cdot f \cdot h.$$

The value of h must be no less than 10 mm. At the selected value of the maximum recording speed, there will be a corresponding maximum frequency f , in Hz, at which segments of the sinusoid are still distinguishable to the naked eye at points of transition across the origin.

For EKG's recording with pen on thermosensitive paper, the requirements of par 19, table 1 must be met within 5 seconds after the recording system is turned on.

3.18 Irregularity of the amplitude-frequency characteristics (par 20, table 1) and the upper edge frequency (par 21, table 1) are determined at the maximum value of sensitivity of the EKG's by recording a sinusoidal signal in the frequency range of 20 to $2f$ Hz and a sequence of orthogonal pulses fed to the input. The width of the pulses in the sequence is 0.2 ± 0.02 seconds. The on-off time is 2. The amplitude of the orthogonal pulses and double amplitude of the sinusoid must

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be equal to 1 mV. Error in determining amplitude must not exceed +2 percent.

The amplitude of the orthogonal pulses A and double amplitude of the sinusoid A_f are measured on the recording (fig 6).

3.19 Irregularity of the amplitude-frequency characteristic in the frequency range lower than f is determined according to the formula:

$$\alpha = \frac{A_f - A}{A} \cdot 100\%.$$

At frequencies higher than f the amplitude-frequency characteristic must fall monotonically.

The upper edge frequency of f is determined by the highest frequency for which the value α remains negative and has the maximum acceptable value.

3.20 The probability of trouble-free operation (par 1.14) is tested at one level of reliability by the method of simultaneous sampling with the acceptable number of failures equal to zero in compliance with GOST 13216-67. Test conditions are governed by GOST 13216-67. After every 100 hours of operation the EKG's are tested for compliance with the requirements of table 1 using the methods of pars 3.7-3.19. An EKG is considered to have passed reliability testing if not one failure occurred during the test period.

During reliability testing, each contact of the commutating unit must close no less than 30 times in 8 hours of uninterrupted operation.

3.21 The rejection coefficient (see note to table 1) is tested at all positions of the lead switch at a sensitivity of 10 mm/mV. The terminals of the lead cables connected to the active electrodes are connected through resistors of $5 \text{ k}\Omega \pm 10$ percent to a common point. When sinusoidal voltage at 100 mV (from peak to peak) is fed between this point and the ground at any frequency within the range of 0.05 to 100 Hz, the amplitude of the signal on the recording (from peak to peak) must not exceed 1 mm.

3.22 The drop in the peak of the transient response (par 22, table 1) is determined at the maximum sensitivity of the EKG's and a rate of recording medium movement equal to 50 mm/s, by recording a discontinuity in constant voltage fed to the input at first positive, then negative, polarity. The duration of feeding of the voltage must be no shorter than 5 seconds.

Plotting is done on the recording (fig 7), and linear dimensions h_1 and h_z are measured. The transient response of each channel must be a monotonic, inverted curvature to the side of the zero line and must not intersect it.

The drop in the peak σ is determined according to the formula:

$$\sigma = \frac{h_z}{h_1} \cdot 100 \text{ percent.}$$

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4. Marking, Packaging, Shipping and Storage

4.1 Attached to each EKG must be a metal plate made in compliance with GOST 12969-67 and containing:

- the trade mark of the manufacturing enterprise;
- standard marking of the EKG;
- the year of output;
- the serial number of the EKG according to the numbering system of the manufacturing enterprise;
- the inscription "Made in the USSR" (for equipment intended for export).

4.2 The metal parts of the structure of the EKG's must be subjected to corrosion proofing in accordance with GOST 13168-69.

4.3 Packaging of the EKG's is governed by GOST 9181-59. Marking of the shipping crate is governed by GOST 14192-71.

4.4 The technical description, certificate and shipping invoice, enclosed in a polymer or polyethylene film, are placed in the shipping crate in accordance with GOST 10354-73.

4.5 Shipment of the EKG's is governed by class S, and storage, by class L of GOST 15150-69.

5. Manufacturer's Guarantees

5.1. The manufacturing enterprise must guarantee the compliance of the EKG's with the requirements of the instant standard when the consumer observes the storage, shipping and operating conditions set by the present standard.

5.2 The guarantee period of the EKG's is no less than 18 months from the day of their placement in operation, and of EKG's intended for export, from the time they cross the national border of the USSR.

Appendix 1

Labeling of EKG Leads

1. The potential lead points must have the following labels:

R--right hand;

L--left hand;

F--left foot;

N--right foot;

C₁--to the right of the sternum at the fourth interspace;

C₂--to the left of the sternum at the fourth interspace;

C₃--at the fifth rib, geometrical midpoint between C₂ and C₄;

C₄--at the fifth interspace on left midclavicular line;

C₅--between C₄ and C₆ along left anterior axillary line;

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C_6 --along left midaxillary line at level C .

2. The electrocardiographic leads must have the following labels:

I--lead from L to R;

II--lead from F to R;

III--lead from F to L.

aVR--lead from R to midpoint LF, formed when the potential lead points from G and F are connected at equal resistance,

aVL--lead from L to midpoint FR, formed when the potential lead points from F and R are connected at equal resistance;

aVF--lead from F to the midpoint RL, formed when the potential lead points from R and L are connected at equal resistance;

V_1-V_6 --lead from C_1-C_6 to midpoint RLF, formed when the potential lead points from RL and F are connected at equal resistance.

Appendix 2

Electrical Equivalent of the Subject

The electrical equivalent of the subject (EES) is used in determining error in measurement of amplitude, the coefficient of relative asymmetry, equivalent resistance of inphase interference, the drift rate of the zero line and the internal noise level.

A diagram of the connection of the EKG to the test signal source to determine the above enumerated parameters is presented in the illustration.

The equivalents of electrode full resistance consist of condensers and resistors connected in parallel. The values of capacitance and active resistance directed to 1 cm² of surface of the electrode interfacing with the uninjured skin of the person being examined are given in the table presented below.

The values of the capacitances and active resistances for the full resistances presented in the chart are determined according to the formulas:

$$R_e = \frac{R'_e}{S_e} ;$$

$$C_e = C'_e \cdot S_e ,$$

where S_e is the electroconductive area of the electrode, interfacing with the subject's skin.

Deviation of the values of resistances and capacitances from the reference values must not exceed the limits of ± 5 percent of the nominal values.

In determining error in measurement of amplitude and the coefficient of relative asymmetry, the electrical equivalent of the subject is connected by switch B1 to the test signal source at inputs R, L, F, N, C_1-C_6 , to which a signal is fed in a pattern and polarity corresponding to table 2 of the instant standard. In

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<u>Site of Electrode</u>	<u>Z_{eq}</u>	<u>$R'_{eq},$ $\Omega \cdot \text{cm}^2$</u>	<u>$C'_{eq},$ $\mu\text{m}/\text{cm}^2$</u>
Forearms and shins	Min.	$3 \cdot 10^5$	0.0166
	Max.	10^6	0.01
Thorax	Min.	10^5	0.0233
	Max.	$2.7 \cdot 10^5$	0.0166

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determining equivalent resistance of inphase interference, inputs R, L, F, N, C_1-C_6 are switched off from the test signal source, and the test signal is fed to input V. The drift rate of the zero line and level of internal noise lead to the input are determined in the absence of the test signal in the position of switch B1 which switches off inputs R, L, F, N, C_1-C_6 .

Switches B2-B10 serve to connect the maximum or minimum values of equivalents of electrode full resistances.

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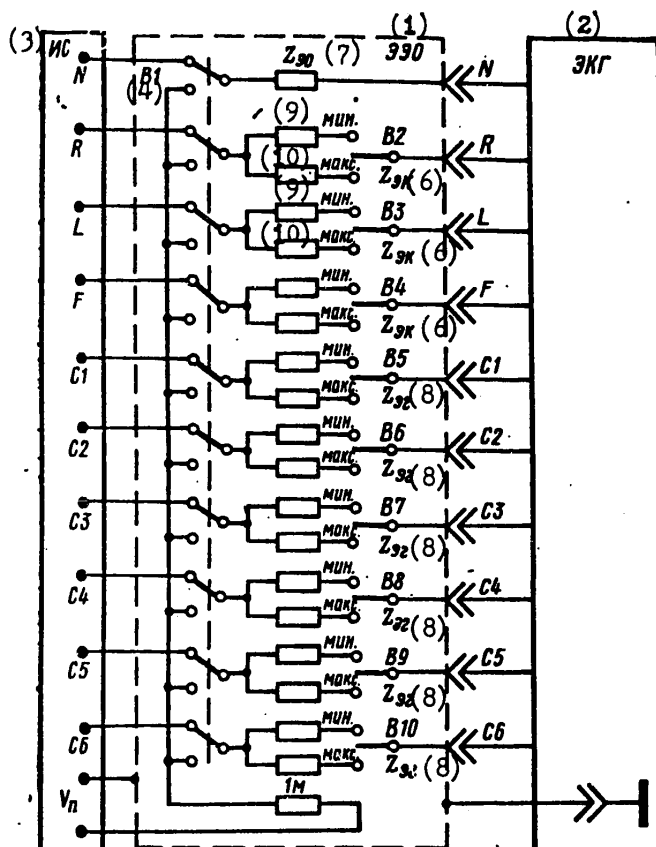


Figure.

Key:

- | | |
|---|--|
| 1. Electrical equivalent of subject | 7. Z_{e0} = equivalent of electrode full resistance at neutral electrodes;
$Z_{e0} = Z_{eq \max}$ |
| 2. EKG undergoing testing | 8. Z_{et} = equivalents of electrode full resistances at thoracic electrodes |
| 3. Test signal source | 9. Minimum |
| 4. B1 = test signal switch | 10. Maximum |
| 5. B2-B10 = switches for electrode full resistances | |
| 6. Z_{eq} = equivalents of electrode full resistances at potential electrodes | |

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MEDICINE

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INITIAL EVALUATION OF CYTOGENETIC ACTIVITY AND POTENTIAL MUTAGENIC HAZARD OF 22 PESTICIDES

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Text Introduction. The development of scientifically substantiated measures aimed at preventing the pollution of the environment with mutagens is one of the immediate tasks of environmental protection in the genetic aspect.

Such a task requires a mass check for mutagenicity of widespread chemical compounds, as well as those planned for an extensive use, including pesticides, for the purpose of detecting and identifying genetically active substances and distributing them according to the degree of potential mutagenic hazard.

The authors were guided by the indicated objective during the performance of this investigation devoted to an initial evaluation of the potential mutagenic hazard of 22 pesticides--representatives of nine classes of chemical compounds--on the basis of the results of their cytogenetic study on mice in accordance with the principle proposed earlier [1], modified in the course of performance of this investigation and briefly set forth in a refined form in the presented report.

Material and methods. The substances for the investigation were selected on the basis of a list of pesticides recommended for application in agriculture by the State Commission on Chemical Agents for the Control of Pests and Diseases of Plants and Weeds. The list of the studied preparations is presented in table 1.

The initial check of pesticides for mutagenicity was made by the method of metaphase analysis of bone marrow cells of white nonline mice, which meet most of the requirements placed upon an object used for mass investigations (relatively low material expenditures, simplicity, availability, good reproducibility of results and a sufficient rate of chromosome analysis). The cytogenetic activity of substances was studied on 2- to 3-month old male mice. Chromosome preparations were made by Ford's standard method in our modification. Pesticides were studied with a single intragastric administration (in the form of a suspension on milk or water emulsion) and bone marrow fixation 20 hours after the effect. Some substances

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were studied after a daily fivefold administration. The amount of the maximum dose of preparations depended on the degree of their toxicity and in each specific case was $\sim 1/2-1/5$ LD₅₀. When a mutagenic effect was detected, the study of pesticides continued up to the ineffective dose. A total of 33,100 metaphases were investigated, including 2,000 in control animals. The difference between the frequency of aberrant cells in experimental and control groups of mice was evaluated by standard statistical methods /2/.

Table 1. List of Investigated Pesticides

Investigated substance	Chemical name	Function
Organochlorine Pesticides		
Kelthane	1,1-di-(4-chlorophenyl)-2,2,2-trichloroethanol	Acaricide
Chlorocholine chloride	(β -ethyl chloride)trimethyl ammonium chloride	Retardant
Euparen	N, N-dimethyl-N-phenyl-N-fluorodichloromethylthiosulfamide	Fungicide
Dithiocarbamic Acid Derivatives		
Cuprocin	A mixture of jointly obtained zinc and copper salts of ethylenebisdithiocarbamic acid in a ratio of 9:1	Fungicide
Polymarcin	A complex of zinc and manganese salts of ethylenebisdithiocarbamic acid with ethylene-thiuramdisulfide in a ratio of 2:1:2	Fungicide
Benzimidazole Derivatives		
BMC	Methyl-N-(2-benzimidazolyl)-carbamate	Fungicide
Uzgen	Methyl ether-N-(1-butylcarbamoylbenzimidazolyl-2) of carbamic acid	Fungicide
Alkyl Ethers of Aryl Carbamic Acid		
Betanal	3-methoxy-carbonyl-aminophenyl-N-(3-methylphenyl) carbamate	Herbicide
Pirimor	5,6-dimethylamino-4-pyrimidinyl-dimethyl carbamate	Aphicide, insecticide
Thiocarbamic Acid Derivatives		
Alipur	A mixture of N-cyclooctyl-N,N-dimethyl urea and BIPC	Herbicide
Vernam	S,N,N-tripropyl-thiocarbamate	Herbicide
Sutan	S-ethyl-N,N-diisobutyl-thiocarbamate	Herbicide
Carboxylic Acid Derivatives		
2M-4X	2-methyl-4-chlorophenoxyacetic acid	Herbicide

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Prefix	2,6-dichlorothiobenzamide	Herbicide
Propanid	3,4-dichloranilide of propionic acid	Herbicide
Ramrod	N-isopropyl-N-phenyl-chloracetamide	Herbicide

Pyridine Derivatives

Reglone	1,1-ethylene-2,2-dipyridylum-dibromide	Arbicide, herbicide
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Phenol Derivatives

Acres	O-isopropyl-O-(2,4-dinitro-6-isobutyl-phenyl) carbonate	Acaricide, fungicide
Karathane	2,4-dinitro-6-(2-octyl)-phenyl crotonate	Fungicide

Organophosphoric Pesticides

Anthio	O,O-dimethyl-S-(N-methyl-N-formyl-carbamoyl-methyl)-dithiophosphate	Insecti- cide
Bromophos	O,O-dimethyl-O-(4-bromo-2,5-dichlorophenyl) thiophosphate	Insecti- cide
Khostathion	O,O-diethyl-O-(1-phenyl-1,2,4-triazolyl-3) thiophosphate	Insecti- cide

Results of investigations and their discussion. The evaluation of the potential genetic hazard of pesticides can be based on the principle of determination of the mutagenic potential of substances according to the following three parameters, which we suggested earlier: degree of manifestation of the effect, level of effective doses and universality of the mutagenic effect /1/. The results of the study of the cytogenetic effect of pesticides on mammals can serve as the basis for their initial evaluation according to the first two indicated criteria.

The degree of manifestation of the effect is an indicator reflecting the relationship between the induced and control levels of mutations, which is established according to the excess of the induced effect over the control level multiple to it and in case of a significant difference is quantitatively equal to this multiplicity. In accordance with this the degree of manifestation of the effect can have the following values: 0--when differences with control are insignificant; 1--when the control level is exceeded significantly; 2--when the twofold control level is exceeded significantly; n --when the n -fold control level is exceeded significantly. If the bone marrow of animals as the object of investigation is designated with the letter symbol "E," the numerical index in it will correspond to the degree of manifestation of the effect ($E_0 \dots E_n$).

The level of effective dose, which, according to the scheme presented in table 2, is determined according to the minimum effective dose with due regard for the degree of its toxicity is the second indicator of the cytogenetic activity of pesticides. The degree of toxicity is evaluated with respect to LD_{50} and is designated as "A" with a dose smaller than or equal to $1/5 LD_{50}$ and as "a" with a dose exceeding $1/5 LD_{50}$.

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Table 2. Scheme of Determination of the Level of Effective Dose

(1) Уровень эффективной дозы		Обозначение уровня эффективной дозы с учетом ее токсичности	
(3) мг/кг	(4) индекс	(5) $<1/5$ ЛД ₅₀	(5) $>1/5$ ЛД ₅₀
<1	5	A_5	a_5
1—10	4	A_4	a_4
11—100	3	A_3	a_3
101—500	2	A_2	a_2
>500	1	A_1	a_1

Key:

- | | |
|--|---------------------|
| 1. Level of effective dose | 3. mg/kg |
| 2. Designation of the level of effective dose with due regard for its toxicity | 4. Index |
| | 5. LD ₅₀ |

The initial characteristic of the potential mutagenic hazard of pesticides is given on the basis of an analysis of the combinations of these basic indices ($B_0—B_n$; $A_5—A_1$, $a_5—a_1$) altogether determining the degree of cytogenetic activity of a substance. On the basis of different combination variants conventionally it is possible to single out six groups of pesticides differing in the degree of cytogenetic activity and, therefore, in the degree of potential mutagenic hazard (table 3).

Table 3. Scheme of Evaluation of the Degree of Potential Mutagenic Hazard of Pesticides According to the Indicators of Their Cytogenetic Activity

Характеристика цитогенетической активности пестицида	Степень потенциальной мутагенной опасности	Характеристика цитогенетической активности пестицида	Степень потенциальной мутагенной опасности
(1)	(2)	(1)	(2)
A_5B_{3-n} ; A_5B_2 ; A_4B_{3-n}	I	A_3B_1 ; A_2B_2 ; A_2B_1	IV
A_5B_1 ; A_4B_2 ; A_3B_{3-n}	II	A_1B_{1-n} ; $a_{5-1}B_{1-n}$	V
A_4B_1 ; A_3B_2 ; A_2B_{3-n}	III	$A_{5-1}B_0$; $a_{3-1}B_0$	VI

Key:

- | | |
|--|---|
| 1. Characteristic of cytogenetic activity of a pesticide | 2. Degree of potential mutagenic hazard |
|--|---|

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The study and initial evaluation of pesticides were made on the basis of such an approach.

The data in the literature on the mutagenic activity of some of the investigated compounds on various genetic objects are presented in table 4.

Table 4. Data on the Mutagenicity of Studied Pesticides (According to the Data in the Literature)

(1) Исследуемое вещество	(2) Мутагенность на различных объектах							(11) Литература
	(3) Микро- орга- низмы	(4) Грибы	(5) Расте- ния	(6) Насе- комые	(7) Клетки животных и челове- ка	(8) Лабораторные животные		
						(9) Цитогенетика	(10) Доминантные летали	
Кельтан (12)	—	0	0	0	0	0	0	[3]
(13) Хлорхолинхлорид	+	0	0	0	0	0	0	[4]
(14) Эупарен	—	0	0	0	0	0	0	[3]; цит. по [5] (15)
(16) БМК	+	+	+	0	+	+	—	Цит. по [5, 6] (15)
(17) Узген (беномил)	+	±	+	0	+	+	—	Цит. по [5, 6—9] (15)
(18) Бетанал	0	—	0	0	0	0	0	Цит. по [5] (15)
(19) Пиримор	0	—	0	0	0	0	0	[10]
(20) Алипур	—	0	0	0	0	0	0	Цит. по [5] (15)
(21) Вернам	—	0	0	0	0	0	0	То же (22)
2М-4Х	—	0	+	+	0	0	0	,
(23) Префикс	—	0	0	0	0	0	0	,
(24) Пропанид	±	0	+	0	0	0	0	,
(25) Рамрод	0	0	—	0	0	0	0	,
(26) Реглон	±	0	+	0	0	0	—	,
(27) Акрекс	—	+	0	0	0	0	0	[11]
(28) Каратан	—	0	0	0	0	0	0	[3]
(29) Антио	0	0	—	0	0	0	0	[12]

Remark. "0"—the substance was not studied; "+"—positive effect; "—"—negative effect; "±"—contradictory data; "+"—colchicine-like effect.

Key:

- | | |
|------------------------------------|----------------------------|
| 1. Investigated substance | 12. Kelthane |
| 2. Mutagenicity on various objects | 13. Chlorocholine chloride |
| 3. Microorganisms | 14. Euparen |
| 4. Fungi | 15. Quoted from |
| 5. Plants | 16. BMC |
| 6. Insects | 17. Uzgen (benomyl) |
| 7. Animal and human cells | 18. Betanal |
| 8. Laboratory animals | 19. Pirimor |
| 9. Cytogenetics | 20. Alipur |
| 10. Dominant lethals | 21. Vernam |
| 11. Literature | 22. The same |

/Key continued on following page/

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- | | |
|--------------|---------------|
| 23. Prefix | 27. Acrex |
| 24. Propanid | 28. Karathane |
| 25. Ramrod | 29. Anthio |
| 26. Reglone | |

It can be seen from the results of the study of the cytogenetic effect of pesticides on bone marrow cells of mice (table 5) that nine substances--betanal, pirimor, (alkyl ethers of aryl carbamic acid); alipur, vernam, sutan (thiocarbamic acid derivatives); prefix, propanid, ramrod (carboxylic acid derivatives) and acrex (phenol derivative)--induced a significant increase in the frequency of aberrant metaphases as compared with control.

As can be seen from the data presented in table 6, these pesticides differ in the degree of potential mutagenic hazard.

Ramrod should be considered the most hazardous (group I). Its maximum cytogenetic effect (4.5%) exceeded the threefold control level significantly and the minimum effective dose (10 mg/kg, $\approx 1/30$ LD₅₀) pertained to the fourth level of effective doses.

Pirimor can be included in group II. It induced a cytogenetic effect in a wide range of doses, including in relatively low (both in terms of weight and toxicity) quantities. The minimum effective dose of pirimor was 2 mg/kg ($\approx 1/50$ LD₅₀). The maximum effect (3.1%) exceeded the twofold control level significantly.

Betanal and acrex also induced a significant excess over the twofold control level. However, their minimum effective doses corresponded to the third level of effective doses, which gave reason to include these pesticides in group III. It should be noted that betanal induced genome mutations, significantly increasing the frequency of polyploid metaphases in the bone marrow of mice.

Propanid was included in group IV. It induced a significant excess over the control level only in the dose of 100 mg/kg, amounting to $1/5$ LD₅₀ (it is the minimum effective dose and corresponds to the third level of effective doses).

Alipur, vernam, sutan and prefix induced a cytogenetic effect of the first degree of manifestation only in high doses (500-1,000 mg/kg), which in all cases exceeded $1/5$ LD₅₀. This gave reason to assume the nonspecific nature of this effect and to include the indicated pesticides in so-called "doubtful mutagens" (group V).

A total of 13 pesticides did not have a mutagenic effect on bone marrow cells of mice and on the basis of the results of the cytogenetic study were included in group VI as the least hazardous compounds.

It should be noted that the conclusion on the degree of potential genetic hazard of the investigated pesticides drawn on the basis of their cytogenetic investigation is tentative and to some extent relative, which is due to the difficulty of presently introducing a parameter making it possible to evaluate the universality of the mutagenic effect. Therefore, at this stage of investigations the practical recommendations with regard to the studied compounds can be only of a temporary compromising nature with a tendency toward underestimating pesticides as components of the mutagenic background of the environment.

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Table 5. Frequency of Chromosome Aberrations in Bone Marrow Cells Under the Effect of the Investigated Pesticides

(1) Исследованное вещество	(2) Доза, мг/кг	(3) Количество исследованных метафаз	(4) Частота метафаз с абберациями, проц.	(5) Число аббераций			(6) p
				всего	на одну метафазу		
					(7)	исследованную	
				(8)	(9)		
Кельтан (10)	100	600	1,00±0,40	12	0,010	2,00	>0,05
(11) Хлорхолинхлорид	50	600	1,50±0,49	12	0,020	1,33	>0,05
	100	600	1,00±0,40	6	0,010	1,00	>0,05
	50	600	1,17±0,44	7	0,011	1,00	>0,05
	50×5	600	0,67±0,33	4	0,006	1,00	>0,05
Эупарен (12)	500	600	1,33±0,47	8	0,013	1,00	>0,05
Купрацин (13)	100	600	1,17±0,44	7	0,011	1,00	>0,05
	1000	600	0,50±0,29	5	0,008	1,67	>0,05
Полимарцин (14)	500	600	1,00±0,41	6	0,010	1,00	>0,05
	1000	600	1,50±0,50	9	0,015	1,00	>0,05
	100	600	1,17±0,44	7	0,012	1,00	>0,05
БМК (15)	500	800	0,75±0,30	6	0,075	1,00	>0,05
Узген (16)	100	800	1,50±0,43	12	0,015	1,00	>0,05
	1000	600	1,17±0,44	7	0,012	1,00	>0,05
	500	600	0,83±0,37	5	0,008	1,00	>0,05
Бетанал (17)	500×5	600	1,33±0,47	8	0,013	1,00	>0,05
	1000	600	3,00±0,69	26	0,043	1,44	△0,001
	100	600	2,67±0,66	18	0,030	1,12	△0,001
Пиримор (18)	50	1000	2,70±0,51	28	0,028	1,03	△0,001
	10	1000	3,10±0,55	34	0,034	1,10	△0,001
	2	1000	2,40±0,48	27	0,027	1,15	△0,001
	0,2	600	1,17±0,44	7	0,011	1,00	>0,05
Алипур (19)	500	600	2,33±0,61	15	0,025	1,07	△0,05
	100	600	1,00±0,40	6	0,010	1,00	>0,05
	50	300	0,33±0,31	1	0,003	1,00	>0,05
Вернам (20)	500	600	3,00±0,69	18	0,030	1,00	△0,001
Сутан (21)	100	600	1,33±0,46	8	0,013	1,00	>0,05
	1000	600	2,31±0,61	14	0,020	1,00	△0,05
2М-4Х	100	600	1,33±0,46	8	0,013	1,00	>0,05
	100	600	1,33±0,46	8	0,013	1,00	>0,05
	50	600	0,33±0,22	6	0,010	3,00	>0,05
Префикс (22)	100×5	600	1,83±0,54	11	0,018	1,00	△0,05
Пропанид (23)	100	600	1,17±0,43	8	0,013	1,14	>0,05
	100	600	2,17±0,59	14	0,020	1,07	△0,05
	10	400	0,75±0,43	3	0,007	1,00	>0,05
Рамрод (24)	100	600	4,50±0,84	27	0,040	1,03	△0,001
	50	600	3,17±0,71	20	0,030	1,05	△0,001
	10	600	2,67±0,66	16	0,027	1,00	△0,001
Реглон (25)	1	600	1,17±0,43	8	0,010	1,10	>0,05
	50	600	1,00±0,40	6	0,010	1,00	>0,05
	Акрекс (26)	100	600	3,00±0,69	18	0,030	1,00
Каратан (27)	50	600	1,50±0,49	16	0,030	1,80	>0,05
	25	600	1,83±0,54	11	0,011	1,00	△0,05
	25	600	1,17±0,43	7	0,011	1,00	>0,05
	12,5	600	1,17±0,43	7	0,011	1,00	>0,05
Антио (28)	5	600	0,67±0,34	5	0,008	1,20	>0,05
	100	600	1,00±0,40	6	0,010	1,00	>0,05
	10	300	1,00±0,57	3	0,010	1,00	>0,05
Бромфос (29)	500	600	1,16±0,43	7	0,011	1,00	>0,05
Хостатион (30)	500×5	600	1,00±0,40	6	0,010	1,00	>0,05
	10	600	1,50±0,49	9	0,015	1,00	>0,05
	1	300	1,00±0,57	3	0,010	1,00	>0,05
Контроль (31)		2000	0,70±0,19	17	0,007	1,00	—

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Key:

- | | |
|--|-----------------|
| 1. Investigated substance | 16. Uzgen |
| 2. Dose, mg/kg | 17. Betanal |
| 3. Number of investigated metaphases | 18. Pirimor |
| 4. Frequency of metaphases with aberrations, percent | 19. Alipur |
| 5. Number of aberrations | 20. Vernam |
| 6. Per metaphase | 21. Sutan |
| 7. Total | 22. Prefix |
| 8. Investigated | 23. Propanid |
| 9. Aberrant | 24. Ramrod |
| 10. Kelthane | 25. Reglone |
| 11. Chlorocholine chloride | 26. Acrex |
| 12. Euparen | 27. Karathane |
| 13. Cupracin | 28. Anthio |
| 14. Polymarcin | 29. Bromophos |
| 15. BMC | 30. Khostathion |
| | 31. Control |

Table 6. Evaluation of the Degree of Potential Mutagenic Hazard of the Investigated Pesticides

(1) Исследуемое вещество	(2) Максимальный цито- генетический эффект		(3) Минимальная действующая доза			(4) Первичная характеристи- ка	(5) Степень потен- циальной мута- генной опас- ности
	Частота абер- рантных мета- фаз, проц.	Оценка	мг/кг	Доля от LD ₅₀	Оценка		
(6)		(7)	(8)	(9)	(7)		
(10) Рамрод	4,50±0,84	B ₂	10	1/30	A ₄	A ₄ B ₂	I
(11) Пиримор	3,10±0,55	B ₂	2	1/50	A ₄	A ₄ B ₂	II
(12) Бетанал	3,00±0,69	B ₂	100	1/25	A ₃	A ₃ B ₂	III
(13) Акрекс	3,00±0,69	B ₂	25	<1/5	A ₃	A ₃ B ₂	III
(14) Пропанид	2,17±0,59	B ₁	100	1/5	A ₃	A ₃ B ₁	IV
(15) Алipur	2,33±0,61	B ₁	500	1/2	a ₂	a ₂ B ₁	V
(16) Вернам	3,00±0,69	B ₂	500	1/4	a ₂	a ₂ B ₂	V
(17) Сутан	2,31±0,61	B ₁	1000	1/3	a ₁	a ₁ B ₁	V
(18) Префикс	1,83±0,54	B ₁	100×5	>1/5	a ₂	a ₂ B ₁	V

Key:

- | | |
|--|---------------------------------|
| 1. Investigated substance | 9. Fraction of LD ₅₀ |
| 2. Maximum cytogenetic effect | 10. Ramrod |
| 3. Minimum effective dose | 11. Pirimor |
| 4. Initial characterization | 12. Betanal |
| 5. Degree of potential mutagenic hazard | 13. Acrex |
| 6. Frequency of aberrant metaphases, percent | 14. Propanid |
| 7. Evaluation | 15. Alipur |
| 8. mg/kg | 16. Vernam |
| | 17. Sutan |
| | 18. Prefix |

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Conclusions. As a result of a cytogenetic screening of 22 pesticides--representatives of nine classes of chemical compounds--nine substances (betanal, pirimor, alipur, vernam, sutan, prefix, propanid, ramrod and acrex) possessing a mutagenic activity of a varying degree of manifestation were detected. A total of 13 pesticides (kelthane, chlorocholine chloride, euparen, cuprocin, polymarcin, BMC, uzgen, 2M-4X, reglone, karathane, anthio, bromophos and khostathion) did not have a cytogenetic effect on bone marrow cells of mice. The investigated pesticides were distributed according to the degree of their potential mutagenic hazard in accordance with the proposed principle.

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"On the Problem of the Mechanism of Spread of a Slow Potential of a Direct Cortical Response," N. G. Eristavi, Institute of Physiology imeni I. S. Beritashvili of the Georgian SSR Academy of Sciences, Tbilisi.

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"Structural Characteristics of Reticular Formation of the Brain Stem," V. V. Amunts, Brain Institute of the USSR Academy of Medical Sciences, Moscow.

"Experimental Models of Emotional Stresses and Their Neurodynamic and Endocrino-Vegetative Correlates," N. I. Velichko, Medical Institute, Khar'kov.

"Impulse Activity of Neurons of the Prefrontal Cortex of Awake Monkeys During Performance of Delayed Responses," M. G. Dashniani and G. I. Machavariani, Institute of Physiology imeni I. S. Beritashvili of the Georgian SSR Academy of Sciences, Tbilisi.

"Correlative Changes in Evoked Brain Potentials During Change in Pain Sensitivity in Rabbits," L. V. Kalyuzhnyy, Ye. V. Golanov, M. A. Kuznetsova and G. V. Torgovanova, Scientific Research Institute of Normal Physiology imeni P. K. Anokhin of the USSR Academy of Medical Sciences, Moscow.

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HUMAN FACTORS

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INFLUENCE OF SOME FACTORS OF SPACEFLIGHT ON HUMAN VESTIBULAR ANALYZER
(ACCORDING TO DATA FROM SOVIET AND FOREIGN PRESS)

Moscow IZVESTIYA AKADEMII NAUK SSSR: SERIYA BIOLOGICHESKAYA in Russian
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[Article by E. V. Lapayev and G. I. Pavlov]

[Text] The article reports the data of investigations of Soviet and foreign scientists in which it was shown that the action of the most common factors of space flight (acceleration, weightlessness, noise, vibration) result in change in the functional condition of the vestibular analyzer. The authors present several theories which explain the etiopathogenesis of adverse reactions, predominantly of vestibular origin, which develop in cosmonauts.

The influence of the most common factors of space flight (acceleration, weightlessness, noise and vibration) has an adverse effect on the human organism and may serve as a cause of reduced fitness for work.

The peculiar functional condition of the vestibular analyzer is considered one of the chief features of the development of such conditions (particularly during the first day of flight).

The most important factors of space flight, the action of which is directly referred to the vestibular analyzer, are acceleration and weightlessness.

It is well known that gravitation underlies the physiological mechanisms of orientation on Earth. All organisms, with the except of the most primitive, react to gravitation either by change in form or change in posture and locomotion. A special organ for perception of gravitation--the vestibular analyzer, which to a great extent ensures spatial orientation--was created in vertebrates and man.

Man and animal easily endure the influence of low intensity acceleration--1, 1.5 gf (Smith and Burton, 1971), which, as a rule, does not produce any biological changes. The mechanism of homeostasis promotes adaptation to it. More intense acceleration induces biological stress, which is manifested by obvious pathological disorders.

Experiments with animals on a centrifuge have demonstrated that changes in posture

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are noted in them after prolonged rotation. In some, termination of the action of acceleration is accompanied by transient disorientation, and ataxia, opisthotonus and somersaulting are observed (Smith and Kelly, 1959; Burton and Smith, 1965). This condition, caused by decreased acceleration, may be arrested by resumption of rotation in the centrifuge. In the opposite case, the indicated postural (attitudinal) reflexes may last for a 12-hour stay under the conditions of terrestrial gravitation. The absence of nystagmus in these cases shows that the described disturbances are not associated with stimulation of the semicircular canals. At the same time the characteristic inverted position of the head makes it possible to hypothesize that stimulation of the otolithic receptor is the cause of the disorientation, ataxia opisthotonus and somersaulting. A similar phenomenon--"the illusion of reversed position"--is noted in a number of people during short term weightlessness and has also been explained (Graybiel and Kelly, 1967) in terms of the features of the function of the otolithic apparatus.

As is well known, the influence of acceleration may give rise to a whole series of adverse symptoms on the part of different organs and systems of the organism and may ultimately affect the human operator's fitness for work. The complex of symptoms developing under the influence of acceleration is chiefly associated with disturbances in the processes of afferent perception, change in the functional condition of the central nervous system and limitation of the mobility of the functioning organs. The role of proprioceptive and vestibular stimulation under the influence of acceleration is acknowledged by all authors.

Under the influence of acceleration, disturbances in the functional condition of the vestibular analyzer set in; the threshold of excitability by galvanic currents and the degree of manifestation of the basic indices of caloric and post-rotational nystagmus change (Yuganov and Gorshkov, 1964; Yuganov, 1965). It has been proved that any influence of overloads of constant intensity, as well as the very process of increasing the intensity of overload, results in activation of the indices of the nystagmus reaction. At the same time the process of decreasing overload appears to be an external agent, resulting in arresting nystagmus. Such effects are explained by the features and unusual nature of functional interactions of the cupular and otolithic apparatuses under conditions of increased gravitation (the action of overloads). With respect to the manifestation and extent of vestibular-sensory and vestibular-vegetative reactions, the prognosis for a person's fitness for work should be acknowledged as favorable under conditions of increased gravitation at the above indicated intensities of acceleration, but not always encouraging in weightlessness (Yuganov and Gorshkov, 1964).

During transition into weightlessness, the cosmonaut's head movements (rotation) result in normal stimulation of the semicircular canals by angular acceleration, however, the resulting sensory information encounters an abnormal type of central vestibular stimulation, caused by the absence of constant stimulation by gravitation.

Many researchers have demonstrated that susceptibility to motion sickness increases in some people during the transition from terrestrial gravitation to weightlessness (Kitayev-Smyk, 1964; Yuganov, et al., 1965; von Beckh, 1961; Gerathewohl, 1956). As it has turned out, adverse reactions during orbital

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flights may be induced both by the absence of gravitational stimulation of the otoliths and by possible stimulation of the semicircular canals during movement of the head and body (Yuganov, 1965). In weightlessness the otolithic organs react to changes in acceleration (Gerathewohl, 1963). After an initial increase in activity in the transitional period, they adapt to zero acceleration, and their bioelectrical activity decreases (Gualtierotti and Bracchi, 1971). Observations during parabolic flights have demonstrated that the manifestation of such reactions as nausea and vomiting are determined by the function of the labyrinth (Graybiel, 1970). Reactions to Coriolis acceleration usually arise in people with normal labyrinths and do not arise in individuals with labyrinth defects (Colehour J., 1964). The illusion of "revolution" also develops only in individuals with a normally functioning labyrinth (Gauer, et al., 1961).

Symptoms of illusory sensations and motion sickness during space flight developed in the astronauts of the "Apollo" spacecraft (Berry, 1973). Illusions of rotation, unpleasant sensations in the stomach, nausea and vomiting were observed.

Unpleasant sensations were also experienced by Soviet astronauts. It is possible that this was caused by the fact that in the absence of gravitation, abnormal afferent signals create a false sensation of rocking and falling and, subsequently, sensations of gastric discomfort, vertigo and nausea. Hydromechanical processes in the semicircular canals also may facilitate the development of spatial illusions, especially sensations of rotation and inverted position (Sjoberg, 1970; Dzendollet, 1971).

The results of Soviet cosmonauts' and American astronauts' space flights indicate that motion sickness developing in some degree of gravitation may be a factor accompanying the state of weightlessness. Deterioration of fitness for work may be a result of this. Thus, during the two first flights to the Skylab Station, the astronauts' work activity was complicated by the development of motion sickness. In some of them the symptoms of this disease developed after they entered the work compartment of the station and after splashdown. The symptoms were observed for 3-5 days in the compartments of the station, although the combination of two drugs (scopolamine and amphetamine) served as a reliable protective measure. An attack of motion sickness also took place on the flight of the third Skylab team. The cause of the decrease in fitness for work is change on the part of a number of the organism's organs and systems, primarily the peculiar functional state of the vestibular analyzer in weightlessness. This condition results in the development of a complex of motion sickness symptoms with practically complete resemblance to sea or air sickness.

One of the most likely causes of the development of space motion sickness is considered to be the influence of Coriolis acceleration of low intensity and long duration against the background of the increasing excitability of the receptor formations of the semicircular canals as the result of weakening of the inhibiting effects of the otolithic apparatus owing to its "functional shutdown."

The shutdown of otolithic apparatus function is recognized as the most likely hypothesis for explaining the mechanisms of the development of adverse vestibular-vegetative disorders (Parin et al., 1962; Sisakyan et al., 1962). Also fairly widespread are the views that under these conditions, change develops in

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the nature and extent of otolithic apparatus stimulation; this change is primarily manifested in a decrease in this stimulation (Parin et al., 1962). Likewise expressed is the viewpoint that under conditions of weightlessness the otolithic apparatus is in a state of peculiar "negative" stimulation (Yuganov, 1965), which in turn affects the activation of the vegetative reflexes from the semicircular canals when the latter are stimulated (Yuganov and Lapayev, 1968).

M. D. Yemel'yanov (1968) feels that there are enough conditions in space flight to disturb the activity of the system of spatial analyzers and that the condition of the higher branches of the central nervous system is the unifying source of such disturbances. The author suggests that the predominance of the stimulating processes in the cerebral cortex under conditions of space flight is conducive to the development of illusory sensations and vegetative disorders.

Thus, the above said suggests that some authors explain the development of the disorders mentioned as the action of weightlessness as an adequate or inadequate vestibular stimulus, and others, as a disturbance, occurring in weightlessness, of the interaction between the otolithic and cupular system or sensory systems providing human spatial orientation.

Some studies present materials on the effect on the vestibular analyzer of hemodynamic changes under the influence of the absence of gravitation. It has been demonstrated that the vestibular analyzer does not remain indifferent to changes of this sort, particularly in redistribution of blood and development of the hypertensive syndrome (Bryanov et al., 1975). Authors feel that the disturbance of hemodynamics with certain microcirculatory disorders on the tissular and microcellular levels, the hypertensive trend of shifts and the disturbances in the water-salt metabolism with tissular unbalance of potassium and calcium ions create the most favorable background for the development of vestibular-vegetative disorders in weightlessness. Against this background, they believe, it is completely possible for pronounced reactions to develop, even in response to threshold and subthreshold vestibular stimuli produced by the motion of the head and trunk during space flight.

The correctness of this and other theories explaining the genesis of vestibular disorders is controversial, but the development of symptoms of motion sickness to some extent during space flight in a number of cases is unquestionable.

It should be noted, however, that one of the most likely vestibular stimuli which may take place in orbital flight is angular acceleration and Coriolis acceleration (Khilov, 1964). They arise during the individual's movements inside the cabin of the vehicle or during unstabilized movement of the latter.

In weightlessness the gravitational forces are absent. So-called immanent accelerations, which arise when work is performed, change a person's apparent weight slightly but have important significance inasmuch as they stimulate the extralabyrinthine mechanoreceptors and consequently increase the flow of impulses to the nerve centers.

Sidelnikov, Solodovnik (1975) feel that the manifestation of vestibulo-vegetative disorders in brief weightlessness and under the conditions of space flight

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basically are a function of two factors: the first is the level of vestibular stability and the second is the level of motor activity of the cosmonaut's head. The combination of these two conditions made it possible to divide all people according to level of vestibular stability under conditions of weightlessness into four groups:

The first group is individuals who do not experience motion sickness in weightlessness, even with high motor activity of the head;

The second group is individuals who experience motion sickness only with high motor activity of the head;

The third group is individuals who experience motion sickness in weightlessness when the head performs a required minimum of movement (in order to perform necessary operator activities);

The fourth group is individuals who experience motion sickness in weightlessness in an immobile state.

At rest and when the head is immobilized physiological deafferentation of the otolith apparatus with subsequent disappearance of tonic, and maintenance of spontaneous or background, impulsation is entirely possible.

Rotating movements of the head provide the same stimulus for the semicircular canals as under terrestrial conditions, but brief linear accelerations developing under these conditions do not cause adequate stimulation of the otolith apparatus. This information cannot be used either for orientation relative to the vertical, or for correlation with afferentation from the semicircular canals. Thus, of all the vestibular extralabyrinthine mechanoreceptors only the semicircular canals are stimulated, essentially by normal movement of the head under terrestrial conditions and in the state of weightlessness alike.

Estimates show that the physical intensity of this stimulus does not exceed $3 \cdot 10^{-5}$ gf (Galle, 1968). The possibility of significant increase in the strength and duration of a given type of vestibular stimulus is due to the promising creation of artificial gravitational forces during interplanetary space flights for the purpose of prophylaxis of undesirable consequences of prolonged stays by man in conditions of weightlessness. It is possible that in the near future artificial gravitation will be produced by the rotation of space stations. In this case, constructions for maintaining normal postural movement at one-third of terrestrial gravitation are adequate to avoid undesirable consequences of angular and Coriolis accelerations arising in the process (Yugannov and Afanas'yev, 1964; Yuganov and Pavlov, 1967; Yuganov et al., 1968).

The results of studies performed in the USSR investigating the effects of low-intensity acceleration of long duration on the human organism make it possible to consider a velocity of 21.2 degrees/s the maximum endurable angular velocity of rotation.

Along with Coriolis acceleration, rotation and angular acceleration of different intensities and durations may also act on the cosmonaut's organism. Cosmonauts

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may encounter the effect of their action during unstabilized flight of the spacecraft and also during ejection. Studies in this direction are basically devoted to searching for the maximum endurable intensities of angular velocities and accelerations according to the time of their action and at different positions of the subject to the axis of rotation.

Of the studies of the latter trend, S. S. Markaryan's series of works (1963, 1965, 1969) must be noted. Markaryan conducted a study of the reactions of a number of organs and systems of the organism under the action on man of angular velocities of 0.25 to 2 rev/s with exposure of up to 20 min and with the trunk inclined 20, 30, 45, 65, 80 and 90 degrees backwards from the vertical axis and lying in a supine position, when the axis of rotation passed through the region of the head or foot. The author investigated the functions of the vestibular analyzer under these conditions, as well as certain indicators of the activity of the cardiovascular and respiratory systems. It was established that increase in the time of the influence and intensity of angular velocities results in a rise in the duration of post-rotation nystagmus and illusions of counter-rotation, with a negative effect on reading of the aeronavigational instruments and the symbols of (Kholinoy)'s table. At the same time an increase in angular velocities from 30 degrees to 120 degrees/s resulted in a decrease in the duration of the illusion of counter-rotation.

The function of the vestibular apparatus is associated with the function of other systems of the organism. Under conditions of weightlessness predominance of the influence of the vagus nerve is sometimes observed. This influence is expressed in bradycardia and gastro-intestinal disorders, which may cause nausea and a feeling of discomfort. At the same time it is known that a stay in weightlessness affects blood circulation and the locomotor apparatus. The combination of all these disturbances may to a still great extent be responsible for the manifestation of symptoms of motion sickness in cosmonauts.

Vestibular stability may also be a function of the conditions of the cosmonaut's stay in a vehicle with a modified gaseous atmosphere. It has been established that respiration of air containing 40-43 percent oxygen and 2 percent carbon dioxide may increase vestibular stability. At the same time, the presence of only 10.5 percent oxygen in the inhaled air decreases vestibular stability in individuals with latent vestibular instability (Markaryan and Sidel'nikov, 1974, 1975; Sidel'nikov, Markaryan, 1974, et al.).

With increase in flight time new problems may also arise. This circumstance increases the significance of future research connected with the action of weightlessness on the human organism. In this connection one of the important tasks of future biomedical research is the study of nervous reflex and sensory changes associated with the condition of weightlessness and transition to it.

Particular attention must specifically be given to cases of development of motion sickness, which is chiefly a function of vestibular reactions to weightlessness.

Recently the view was expressed that motion sickness is the manifestation of a pronounced crisis of parasympathetic nature developing under prolonged stimulation of certain afferent systems (visual, auditory, interoceptive, etc.), chiefly the

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vestibular, in people having constitutionally acquired insufficiency of the limbico-reticular system (Yuganov, Solodovnik, 1976). The connection between individual susceptibility to motion sickness on Earth and in weightlessness is still unclear (Graybiel, et al., 1973); the combined action of weightlessness and other environmental conditions, such as microclimate, sensory deprivation, limited mobility and emotional factors, is also unknown.

Presently existing high gravitation engines for piloted space flights entail the development of noise and vibration factors which raise the problem of protecting the crew of the spacecraft from them.

The fields of acoustical energy created by space systems have a sufficiently high level and may disturb normal human activity, cause auditory disturbances, reduce fitness for work, alter physiological functions, etc.

The reactions of the auditory analyzer play the leading role among the physiological effects of the action of noise. Their influence on the vestibular apparatus has not been ruled out, however. Subjective reports of disorientation, vertigo, nausea and disturbances in postural balance indicate that high intensity acoustical energy may be a stimulus to the vestibular apparatus (Borshchevskiy, et al., 1967). Studies substantiating the causes of vestibular responses to the action of noise indicate that the vestibular apparatus may be the object of acoustical stimulation (Parker, et al., 1968; Harris, 1971).

In addition to the vestibular apparatus, noise levels of 140 dB or more also act on other sensory systems and possibly cause a drop in fitness for work of reflex activity of the mechanoreceptors and proprioceptors (Yuganov, et al., 1966; Krylov et al., 1968). Regardless of the mechanism of direct influence of intensive noise on the auditory apparatus or on the auditory apparatus and the mechanoreceptors, the presence of complaints of loss of orientation, vertigo, nausea and other symptoms indicate the stimulating effect of acoustical energy on the vestibular system.

In orbital space flight noises arising during operation of different assemblies and life support systems act continuously on the cosmonaut. In prolonged flight the factor of the uninterrupted nature of the influence has a substantial significance (Krylov, 1965).

During flight on a spacecraft, considerable vibration may arise (Guignard 1972); this vibration is caused by the operation of the main engines and the functioning of the auxiliary power equipment.

Vibration is transmitted to the cosmonaut directly through supporting surfaces such as the seat, headrest and control lever. The main parameters of vibration, which determine its influence on man are frequency, intensity (amplitude), direction with respect to the anatomical parts of the body and the duration of influence.

The posture in which the cosmonaut is positioned and secured in his seat is conducive to the transmission of spacecraft vibrations to the trunk and head without damping (Taub, 1966; Schoenberger, 1968). Despite the high thrust of the

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rocket during the launching of the Apollo spacecraft, vibrations arising at that time were noted by the astronauts, but no serious discomfort was caused (Berry, 1969).

In weightlessness, the flight seems motionless and smooth, however, vibrations from secondary sources, such as the life support systems, for example, may be noted visually or by touching the inner sheathing of the vehicle. Even at low intensity, when constantly active during prolonged space flight, the vibrations may lead to undesirable consequences.

The dermal receptors serve as the main vibration-sensitive formations; they contain vibrotactile sensory elements (McIntyre, 1965; Moore, 1966), mechanoreceptors lying in the deeper structures (particularly in the muscles, tendons, joints and internal organs) (McIntyre, 1965; Guignard, 1972) and the vestibular apparatus (Borshchevskiy, Krylov; Benson, 1965; Guignard, 1972).

It is known from the data in the literature that undesirable reactions of vestibular origin may arise during fluctuations from velocities of 0.1 to 1 Hz (Guignard, 1972). Accumulation of such fluctuations may result in the development or stronger manifestation of motion sickness symptoms. The manifestation of these symptoms depends on the individual's original condition.

Flight experience, as well as certain laboratory experiments, have shown that strong low-frequency vibration may also disturb human fitness for work in a nonspecific manner, following the pattern of a distracting and fatiguing agent like noise (Guignard, 1972).

The enumerated factors of space flight may act both independently and in combination with each other and with other factors. In the case of combined action of stress factors, as often occurs in space flight, additive synergistic or antagonistic effects may develop (K. K. Ioseliani, 1967; Grether, 1970; Wilkinson, 1969; Guignard, 1972; Harris and Sommer, 1973).

Thus, the studies of Soviet and foreign authors have shown that the action of the most common dynamic factors of space flight (acceleration, weightlessness, noise, vibration) result in perceptible shifts in the functional condition of the vestibular apparatus. This in turn may result in the development of adverse reactions, predominantly of vestibular origin; this ultimately affects the cosmonauts' fitness for work.

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MODELING PILOT CONTROL ACTIVITY

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[Article by V. A. Kondratenkov]

[Text] One of the most radical means of increasing the effectiveness of the functioning of erg control systems (ECS) controlling the flight of aircraft is rational distribution of control functions between the pilot and the automatic devices--in other words, the provision of a level of automation and (within the scope of this level) a method of distributing functions with which the global extremum of a given generalized criterion of the quality of the ECS is obtained (1).

With a specified list of control tasks, an analytical search for a rational distribution of functions is possible only when models of pilot behavior corresponding to the given list are available as parts of the ECS. Here it is very important for the pilot behavior models to be sensitive to the level of difficulty of performing the control process, since the "human component" of the optimized, generalized quality criterion is most commonly the pilot's level of psychophysiological tension.

Without setting ourselves the goal of critical analysis of known and widespread models of pilot behavior, we shall note that models based on the methods of statistical identification of the pilot's transmission function (2, 3) and the method of generalized work characteristics of the human operator (4) are the most appropriate for solving the task of the analytical search for a distribution of control functions. Use of these methods, however, is significantly limited by the requirement of observability of the pilot's "input coordinates," i.e., it may be applied only to a narrow class of control tasks in solving which the pilot receives information only from instrumental displays. Moreover, the methods of statistical identification require the presence of a steady state quality in the random processes of adjustment of the control levers by the pilot--something that occurs in extremely rare cases--and do not give the pilot behavior models information on the "human component."

Another method is presented for modeling the behavior of a pilot performing the process of aircraft flight control, proper, i.e., stabilization of specified and generally variable values of the flight parameters. This method, which is free of the above noted limitations, is based on current concepts in engineering psychology concerning the mechanisms of the action of the pilot's psychological

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structures in flight control, namely: regardless of the nature of the information presented, the pilot responds with a suitable adjustment $y(t)$ of the control level to the appearance of discrepancies between the conceptual flight model (i.e., the system of notions of how the flight should proceed) and the operational flight pattern (i.e., the system of notions of how the flight is, in fact, proceeding) (5). Modeling of the random processes $y(t)$ of adjustment of the control levers equivalent to the given discrepancy between the conceptual model and the operational flight pattern will hereinafter be called modeling of pilot control activity.

As indicated by analysis of realizations $y_k(t)$ of random processes $y(t)$ recorded by the flight information recorders of the aircraft, the $y(t)$ are generally nonsteady-state processes. It is also generally impossible to express $y_k(t)$ through a given steady-state random function.

Hence the following transform was used:

$$y_k(t) = Y_k(t) + y_k^0(t), \quad (1)$$

where $Y_k(t)$ is the random, generally nonsteady-state function obtained by applying to the $y_k(t)$ an operation equivalent to low-frequency filtration; $y_k^0(t)$ is the centered function satisfying the steady-state and normal ergodicity tests.

The component $Y_k(t)$ may be regarded as deliberate, basic adjustment of the control lever for the purpose of eliminating discrepancies between the conceptual flight model and the operational flight pattern (6). Statistical analysis of nonsteady-state random processes $Y_k(t)$ demonstrated that their frequency structure is not due to the performance of the aircraft as an object of control, consequently, to the level of the difficulty of performing the control process for the pilot. This was noted by M. A. Kotik (7), who established that the more experience the pilot has, the closer in size are the integral ratings $\int_0^t y_k(t) dt$. But owing to (1)

$$\int_0^t y_k(t) dt = \int_0^t Y_k(t) dt;$$

it follows that as the pilot acquires experience the component $Y_k(t)$ bears increasingly less information about the pilot. Hence, it is no accident that we propose replacing an experienced, trained pilot performing adjustment $Y(t)$ of the control lever with an optimal controller.

As the research shows, the "human component" is introduced to pilot control

activity by the component $y(t)$ (owing to the ergodicity of $y_k(t)$, we drop the "k" index) which is a combination of adjusting and maintaining movements, as well as tremor (6). The experimentally determined function of the spectral density of the $y(t)$ processes when the pilot solves any operational flight control task

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is approximated with sufficient accuracy by the analytical expression:

$$s_y^0(\omega) = \frac{\sigma_y^2}{\pi} \alpha \frac{\alpha^2 + \beta^2 + \omega^2}{(\alpha^2 + \beta^2 + \omega^2)^2 - 4\beta^2\omega^2}, \quad (2)$$

where σ_y^2 is the dispersion of the $y(t)$ process; α is the damping coefficient of the self-correlated function of the $y(t)$ process; β is the parameter of the self-correlated function characterizing the frequency structure of the $y(t)$ process.

The values σ_y^2 , α and β proved to be extremely sensitive to the performance of the aircraft as an object of control and minimal in the range of performance values optimal for the pilot (weather conditions, the proximity of the Earth, the size of the angle of bank during turns, the take-off and landing mass of the aircraft, etc.).

The idea occurs of modeling pilot control activity by a combination of reactions $Y(t)$ of the optimal controller to discrepancies between the conceptual flight

model and the operational flight pattern and $y(t)$ reactions of the shaper filter to a wide-band signal, for example, to "white noise." Consequently, the described method of modeling pilot behavior consists of synthesizing the controller with the output coordinate $Y(t)$ and the shaper filter which transforms "white noise" into a random signal with spectral density (2).

Synthesis of the controller with the output coordinate $Y(t)$ is essentially a simple procedure when information is available on the input signal, in our case--concerning the nature and size of the discrepancy between the conceptual flight model and the operational flight pattern. Statistical analysis of the components of $Y_k(t)$ relating to the different elements of flight made it possible to observe the following two features.

First, under transitional control conditions, characterized by significant changes in $Y(t)$, the $Y_k(t)$ curves may be regarded as the reaction of some dynamic system to a standard signal in the form of a stepwise function or orthogonal pulse. Thus it is possible to accept the hypothesis that the discrepancy between the conceptual flight model and the operational flight pattern is for the pilot a standard input signal in the form of a stepwise function or orthogonal pulse.

Second, using factor analysis, it is possible to establish the basic parameters which determine the nature of change in the transient functions $Y_k(t)$ (but which do not affect their frequency structure). The significance of the amplitude of the discrepancy between the conceptual flight model and the operational flight pattern is assigned to the X values of these parameters. Aircraft mass during take-off, the angle of inclination of the trajectory during the performance of transitional operations in changing flight altitude, and the size of the angle of bank during turns may be cited as examples of basic parameters.

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The following method may conveniently be used in obtaining models of realization by the pilot of component $Y(t)$.

First of all, it is necessary to have a sufficiently representative group of realizations $Y(t)$, $k=1, 2, \dots, n$, performed by pilots of a roughly identical level of training in solving an identical task of piloting and corresponding to one value X_i , $i=1, 2, \dots, l$, of a basic parameter of the given piloting task. Computing the average for the group from n realizations and attributing it to value X_i , we obtain a unitary, averaged, transient function $Y_i(t)$. Performing this same operation with groups of realizations corresponding to l values of the basic parameters, we obtain l unitary averaged transient functions. If all of the l functions are sufficiently close to each other, it is expedient to obtain a relative transient function $Y(t)$ as the average of l unitary averaged transient functions.

Synthesis of the transmission function of the controller which realizes the transient function $\bar{Y}(t)$, may be accomplished by known methods based on approximation of $\bar{Y}(t)$ by solving differential equation (9), assuming that the input influence of the controller is unitary.

The task of synthesizing the shaper filter which transforms a wide-band random process into a process with spectral density (2) is comparatively simple, since spectral density (2) is a rational function of frequency ω . Two conditions of physical feasibility of the required shaper filter--the continuity of function

$S_0(\omega)$ and the (Peli-Vinera) condition (10)--are met automatically, since the denominator (2) has no real root, and the (Peli-Vinera) condition amounts to a

requirement that the expression $\frac{\ln \omega}{1+\omega^2}$ be bounded when there is an unbounded increase in ω . What is more, it can be shown that the required shaper filter is minimum-phase. Then, using method (11), we obtain an expression for the transmission function $W_\phi(p)$ of the shaper filter which transforms a "white noise" signal with an intensity of N_0 into a signal with spectral density (2):

$$W_\phi(p) = \sigma_\nu^0 \sqrt{\frac{\alpha}{\pi N_0}} \frac{p + \sqrt{\alpha^2 + \beta^2}}{p^2 + 2\alpha p + \alpha^2 + \beta^2}, \quad (3)$$

where σ_ν^0 , α , β are values in expression (2).

Thus, the parameters of the shaper filter (3) are a function of the pilot's tension level.

Let us cite the example of synthesis of a model of the control activity of a pilot turning an aircraft by coordinated deflection of the control lever in the elevator ($y_B(t)$) and the aileron ($y_A(t)$) channels. In order to obtain a model, we selected groups of realizations $y_k(t)$, corresponding to performance of turns by experienced pilots at practically identical values of flight altitude and velocity and engine operating conditions. Only the values of the angle of bank γ , were different, thus the value of γ was taken as the basic parameter.

Relative transient functions were determined for the transient turn conditions:

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entering turn--

$$\bar{Y}_s(t) = -0,005 - 0,1249t + 0,00375 \sin 0,4488t + 0,0507 \sin 0,8976t - 0,0193 \sin 1,3464t, \quad (4)$$

$$\bar{Y}_s(t) = -0,0279 + 0,1496t + 0,13137t^2 - 0,07589t^3 + 0,012317t^4 - 0,000656t^5;$$

coming out of turn--

$$\bar{Y}_s(t) = -0,879 + 0,1463t - 0,03083 \sin 0,5236t - 0,0774 \sin 1,0472t + 0,00547 \sin 1,5708t, \quad (5)$$

$$\bar{Y}_s(t) = 0,0227 - 0,5417t + 1,11733t^2 - 1,1273t^3 + 0,53682t^4 - 0,12823t^5 + 0,015t^6 - 0,0006848t^7.$$

Using known methods (9) we obtain the transmission functions of the controllers realizing the transient functions (4) and (5) during individual perturbations:

entering turn--

$$H_s(p) = -\frac{0,879}{(1 + 1,179p)(1 + 0,703p)(1 + 0,39p)(1 + 0,271p)}, \quad (6)$$

$$H_s(p) = \frac{1,4835}{1 + 4,1373p + 3,6699p^2 + 3,2287p^3};$$

coming out of turn--

$$H_s(p) = -\frac{0,879}{(1 + 0,705p)(1 + 0,404p)(1 + 0,29p)(1 + 0,231p)}, \quad (7)$$

$$H_s(p) = -\frac{0,6952}{1 + 2,7273p + 2,3309p^2 + 1,5189p^3}.$$

The structure of the transmission function of the shaper filter which generates the $\bar{y}_s(t)$ and $\bar{y}_a(t)$ processes remains unchanged for all elements of turn performance and has the form of expression (3). Adjustment of the σ_y^0 , α , β parameters lead to the following algorithms (γ is in degrees):

elevator channel

$$\begin{aligned} \sigma_y^0 &= 2,102 + 0,1543\gamma - 0,00244\gamma^2 + 0,0000167\gamma^3, \\ \alpha &= 5,818 - 0,4312\gamma + 0,0097\gamma^2 - 0,0000503\gamma^3, \\ \beta &= 10,515 - 0,1509\gamma + 0,00275\gamma^2 - 0,0000143\gamma^3; \end{aligned} \quad (8)$$

aileron channel

$$\begin{aligned} \sigma_y^0 &= 2,562 - 0,1304\gamma + 0,00286\gamma^2 - 0,000015\gamma^3, \\ \alpha &= 2,029 + 0,0406\gamma - 0,00079\gamma^2 + 0,0000058\gamma^3, \\ \beta &= 5,3 + 0,0651\gamma - 0,001\gamma^2 + 0,0000087\gamma^3. \end{aligned} \quad (9)$$

Imitation of the model of (6), (7) and (3), (8), (9) on a computer gave a sufficiently good convergence with recordings of real flights. The proposed method is free of limitations on the structure of random processes and the nature of the pilot's "input coordinates" and gives the pilot behavior models information on the "human component".

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Summary

A method is suggested for modeling the monitoring activity of pilots. It is based on separate consideration of components in the random processes of control level movement. The model is sensitive to the level of difficulty of control for the pilot.

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PSYCHOLOGY

CORRELATIVE PARAMETER OF ELECTROENCEPHALOGRAM IN PRESENCE OF EMOTIONAL STRESS

Baku KORRELYATSIONNYYE POKAZATELI ELEKTROENTSEFALOGRAMM GOLOVNOGO MOZGA PRI EMOTSIONAL'NOM STRESSE in Russian 1979 (signed to press 18 Jan 80) pp 8-54, 102-122

[Chapters 1, 2 of Section I and Chapter 1 of Section II from book "Correlative Parameters of Electroencephalograms of the Brain in the Presence of Emotional Stress" by Arif M. Mamedov, Scientific Research Institute of Normal Physiology imeni P. K. Anokhin, USSR Academy of Medical Sciences, and Institute of Physiology imeni A. I. Karayev, Azerbaijan Academy of Sciences, Izdatel'stvo "Elm", 1200 copies, 129 pages]

[Text] Section I

Chapter 1. Pressing Problems of Emotional Stress

The conception of H. Selye [87, 88], the initial theses of which were formulated as far back as 1937, concerning stress deals primarily with its endocrine and biochemical aspect. The term, "stress," introduced by that author referred to the general adaptation syndrome which develops in an organism in response to various stimuli. "Nonspecificity" of reactions arising in response to any stressor, regardless of its nature, is the most typical feature of this syndrome. In all such cases, which are associated with a change in the body's defense systems, a stereotype reaction appears in the form of faster pulse, respiration, palpitations and elevation of arterial pressure. These changes are associated with intensification of activity of the hypothalamo-pituitary complex which secretes ACTH which, in turn, "prompts" the adrenal cortex to produce corticoid hormones.

As a rule, these reactions take place in three stages: 1) brief "alarm reaction," "call to arms" of defenses of the organism; 2) stage of adaptation which, so to speak, reveals reserves; 3) after prolonged and continuing exposure to stimuli the achieved adaptation is again lost and the organism goes into the "depletion stage."

Selye's theory prompted numerous studies of pituitary-adrenal correlations in the presence of stress.

Thus, some authors [58] attribute the leading role in adaptive reactions to stress conditions to the adrenosympathetic system, others [100] to the

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hypothalamo-pituitary area, i.e., the junction between the nervous and endocrine systems, while others yet attribute it to epinephrine discharged into blood which affects the hypothalamus causing secretion of ACTH, the hormone of the anterior hypophyseal lobe.

In the complicated complex of neurohumoral and endocrine components of the adaptation syndrome of H. Selye, least studied are the relations between nervous processes in the cortex and subcortical structures of the brain.

Numerous studies of recent years proved the existence of certain correlations between nervous and humoral processes. For example, it was established [41] that, in the presence of stress states, maximum concentration of corticosterone in the cerebral cortex and hypothalamus is associated with intensified synchronization of EEG theta waves. During specific periods, a correlation is observed between these parameters, which is indicative of the leading role of the hypothalamus in forming emotional states. Correlation analysis revealed that under conditions of emotional stress there is significant increase of R/T index on the EKG associated with accentuation of EEG theta rhythm. The link between accentuation of autonomic reactions of the organism and intensification of theta activity is consistent with the conception of P. K. Anokhin and A. I. Shumilina [8, 111] concerning the adreno-sympathetic basis of theta rhythm--"tension rhythm" [10].

At the present time, the humoral aspect of these mechanisms has been described comprehensively and thoroughly enough in numerous works and studies. However, as the problem was studied, it became necessary to pay special attention to the nervous mechanisms of these phenomena. In recent years, the authors of a number of scientific publications correctly indicated that stress is primarily a reaction of the nervous system to deleterious factors, with secondary expression by changes in autonomic and hormonal parameters [96, 89, 130, 104].

However, most authors interpret differently the nervous mechanisms of formation of emotions.

At the start of the 20th century, the theory of James-Lange prevailed of "peripheral" origin of emotions, according to which emotional sensation was related to visceral and muscular reactions. It was indicated that emotions arising as a result of functional changes in internal organs are the consequences of the latter, and not their cause. These authors, who focused their attention on the "periphery" [139, 144], were unable to disclose the central mechanism of appearance of emotions.

The conception of central nervous substrate of formation of emotional states was first advanced in the works of Sherrington [156], Bard [123] and Cannon [128]. They attributed the leading significance to subcortical structures of the brain, chiefly the thalamus. However, the emphasis that the authors laid on central mechanisms of formation of emotions did not enable them to demonstrate the real mechanism of central-peripheral correlations of emotional reactions. The common flaw of the main theories of emotions was the lack of the biological aspect of the question of emotional states as a valid fact of nature, as the product of evolution that enabled animals to adapt to environmental conditions.

According to biological theory of emotions of P. K. Anokhin [9, 34], negative emotional tensions arise when the model prepared in advance of future events, which is programmed in the acceptor of action results, does not coincide with the

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parameters of the results of a behavioral act (Figure 1). Emotions, as subjective sensations, were fixed in the course of complex evolutionary development. As a result of useful reactions, emotion changed into an inseparable part of the organism's reaction when there was a need for food, exposure to various stimuli, including deleterious factors. Emotions enabled living things to rapidly assess the effect on the organism of various exogenous stimuli, their endogenous needs and results of behavioral activity. Any need is associated with a negative emotional experience (alimentary, defense) which mobilizes the organism for action aimed at satisfying the arising need. "Emotion is the most refined [precise] coordinated course of central and peripheral processes..., this complex unfolds, because of its morphogenetic origin and physical distinctions, as an integral functional system (Figure 1) with all its inherent patterns that unite the cortex and diencephalic system" (P. K. Anokhin).

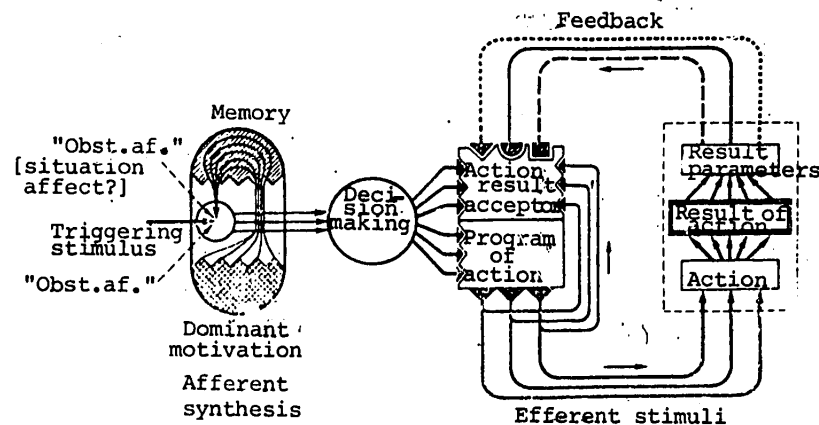


Figure 1. Functional system of P. K. Anokhin

P. V. Simonov [90] advanced the "information theory of emotions." According to this theory, the emotions of animals and man reflect the magnitude of need and probability of satisfying it at a given time. The degree of emotional tension (E) depends on the strength of the need (N), as well as difference between information that is prognostically necessary to satisfy the need (In) and information that really exists (Ir):

$$E = N(In - Ir)$$

A shortage of pragmatic information, i.e., information as to how to proceed in a difficult situation that requires mobilization of all of the organism's forces, leads to appearance of negative emotions that are actively minimized by the subject. And it is quite sufficient for the semantics of the goal ("acceptor of action results") not to coincide with the actually obtained results. When the gained information exceeds the previously present forecast [prognosis], there is activation of the nervous system of positive emotions.

As we know, gradual approximation of a signal that is reinforced (circle) and not reinforced (ellipse) with food, leading to a shortage of information, was used

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by the Pavlovian school as one of the effective procedures for neurotization of experimental dogs. The conception of M. M. Khananashvili [105] concerning information neuroses discloses pathology of higher nervous activity that arises when the brain is overloaded with information, there is a prolonged shortage of information, as well as when it is necessary to analyze a large number of conditioned stimuli organized in stereotype or probability systems.

Pribram [155] observes that a low probability of reinforcement by action of a need of the organism is the cause of negative emotions. This author indicates that it is better to call emotion theory "theory of uncertainty," or "theory of dependence of emotions on degree of uncertainty." Hodge [136] concluded, as far back as 1935, that emotions arise when expression of an adequate response to a present situation is impossible or doubtful. Emotion is the force of a need reflected by the brain. Similar theoretical theses were expounded in other works [131, 122]. Thus, analysis of the above-mentioned theories and conceptions indicates that nervous and mental factors play the leading role in the genesis of the adaptation syndrome. These facts are reflected in the neurogenic theory of essential hypertension expounded by P. K. Anokhin [5, 9] and G. F. Lang [56].

Thus, G. F. Lang indicated that emotional tension of higher nervous activity leads to attenuation of the regulatory influence of the cortex on the hypothalamus, as a result of which excitability of the latter is heightened. Such correlations between the cortex and hypothalamus increase descending pressor influences.

The importance of the psychophysiological aspect of emotional stress was noted at the Stockholm Symposium on Stress [58], where attention was focused merely on consideration of autonomic manifestations of the organism, biochemical changes in end metabolic products in blood, etc.

The conditioned reflex method (I. P. Pavlov), which became classical, proved that processes occurring in viscera depended on brain activity. The important role of the cerebral cortex in function of the endogenous environment was proven by V. M. Bekhterev [23] by the method of electric stimulation of the brain. L. A. Orbeli [80], the author of "Theory of Adaptive and Trophic Role of the Sympathetic Nervous System," made a major contribution to development of physiology and pathology of the autonomic nervous system.

Thus, the neurogenic mechanism is important to studies of this problem.

What are the conditions that cause formation of emotional stress and its change to a "static form"?

In the opinion of K. V. Sudakov [97, 98], intensive scientific and technological progress of the last century created some serious preconditions for a rise in neuropsychological and cardiovascular diseases. However, no "insane pace of modern times, no acuteness of nervous vestiges can cause hypertension, if this is indeed a pace where periods of maximum tension alternate with moments of calm" [97, 98b).

I. P. Pavlov [83] had already demonstrated that life is based on the enduring alternation of actions, recurrent life cycles (sleep, wakefulness, work, rest, etc.)--the dynamic stereotype. The basis of the dynamic stereotype is formation in the brain of a certain stable sequence of rhythms of two main processes, excitation and

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inhibition. Thus, optimum conditions are created for the organism's useful adaptive reactions under specific, constant environmental conditions. However, I. P. Pavlov stressed that alteration of the stereotype, particularly of its stable, fixed form, is always associated with "tension [strain] of excitatory and inhibitory processes."

It must be noted that tension of the organism formed under different conditions is not a strictly pathological process [39, 40].

Brief, moderate neuropsychological tension, which developed in the course of evolution for emergency action under difficult conditions, is adequate for the organism and takes place with utmost efficiency. This is associated with acceleration of mental processes, which is interpreted as a sign of heightened adaptation properties of the organism with regard to stress. Under such conditions, the organism reacts, first of all, in the form of a change in lability of nervous processes [39, 40].

It is known [40] that moderate emotional stress has a beneficial effect on short-term memory. H. Selye maintains that brief moderate stress is really not dangerous to the organism. Moreover, it is necessary to condition or train the body, to enhance its nonspecific resistance.

However, the change of emotional excitation into a "static" form is the main and initial pathogenetic factor in formation of various pathological changes in the organism. According to the conception of P. K. Anokhin, "static" negative emotional excitation involving corticohypothalamic and limbic structures plays the leading role in onset of essential hypertension. The cardinal theses in P. K. Anokhin's biological theory of emotions enables us to comprehend the basic mechanism of appearance of "static" emotional excitation leading to breakdown of the powerful systems of self-regulation of physiological functions.

Prolonged excitability of nervous elements with broad involvement of other nervous structures, progressive increase in amount of stimulating hormones in blood "breaks" the mechanisms of self-regulation of functional systems of the organism and changes the course of a "pathological" emotion into a chronic form, on the order of a "vicious circle."

We know that interaction between the nervous and cardiovascular systems, which developed as a result of many centuries of evolution, is important to implementation of normal vital functions, adaptation of the organism to rapidly changing environmental conditions [107]. However, in the last few decades, because of information overloads, situations arise more and more often, in which man has more "unreacted emotions" associated with nervous or mental tension, "emotional stress" appears and leads to disruption of nervous regulation of the function of different systems of the organism, including the cardiovascular system.

Thus, when man or animal cannot, for some reason, satisfy their social or biological needs for a long time, they develop a sort of "conflict" that is associated with constant build-up of dissatisfaction, irritation and emotional tension. Such situations were named "conflict situations." A prolonged "conflict situation" generates "emotional stress," which causes appearance of "static" negative emotional excitation under chronic conditions [97].

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At present there are various methods for studying emotional stress in experimental "conflict situations": the method of instrumental conditioned reactions, prolonged intensive stimulation, repeated use of "signal" or "nonsignal" nociceptive stimuli, electric stimulation of emotiogenic structures of the brain, situation of anticipation of unpleasant factors, particularly under conditions of "prognostic uncertainty," simultaneous presence of several emotionally significant factors, etc.

In the experiments of Henry et al. [135], a "conflict situation" caused constant fights and tension in mice, which led to persistent arterial hypertension after a few days.

Analogous data on "conflict situations" related to anticipation of unpleasant factors were obtained in other studies [77].

Prolonged manifestation of changes inherent in emotional stress is caused by the presence of neuronal interaction between the prosencephalon and stem. Indeed, exclusion of the corticoreticular element reduces significantly the duration of the aftereffect reaction to strong nociceptive stimuli [62].

Interestingly enough, animals develop persistent tension the most often when electrocutaneous stimulation is preceded by an instrumental reaction. The very procedure of electrocutaneous stimulation led only to brief reactions [119, 109]. Thus, one of the mechanisms of activation and prolonged persistence of an emotional state is conditioned reflex temporary association, which is formed very rapidly and becomes static under the influence of "negative" stimuli. In this case, prolonged retention of traces of conditioned reflex excitation indicates that emotional states are also instrumental in activating the mechanisms of long-term memory, thus causing prolonged persistence of pathological, obsessive reactions in the presence of neurosis [104, 105].

It has been established that onset of emotional stress in "conflict situations" is enhanced in the presence of other factors (cooling, psychophysical loads, immobilization).

Immobilization of animals for many hours acts like a very effective psychoemotional stressor, which elicits the typical stress reaction (rage, fear) with all its functional and morphological manifestations. Immobilization of monkeys in the presence of dominant aggressive-defense excitation leads to extreme accentuation of negative emotion, which is associated with circulatory disturbances. Repeated experiments (starting with the second) led to stabilization of pathological changes. Several authors [112] have demonstrated stabilization of changes in bioelectrical activity of the limbico-hypothalamic structures of animals in the case of recurrent immobilization stress.

The level of emotional tension and degree of its manifestation are regulated by altering the probability of using and reinforcing signals [86]. Thus, a decrease in number of stimuli in an integrated system that are reinforced in random order and increase in number thereof with stereotype reinforcement diminish emotional tension and can prevent development of neurosis. Some animals independently choose the stereotype program of behavior, which could be interpreted as manifestation of self-regulation of the level of emotional tension.

Rats submitted to unavoidable nociceptive stimuli preferred the half of the chamber from which came the signal giving warning of the electric shock, which enabled them to prepare somehow for the negative sensations [153].

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With irregular and repeated use of an electrocutaneous stimulus, the animals were in a constant negative emotional stress state, which led to severe dystrophic disorders. Interestingly enough, in the case of random delivery of electrodermal stimuli (5-6 mA) the rats developed several times more ulcerations of different organs than in experiments in a signal situation [163, 164].

Analysis of the EEG and autonomic parameters of rabbits (1) revealed that numerous electrodermal stimuli preceded by a photic signal led to considerably less development of a stress state than in a situation without signals.

The data of K. V. Sudakov et al. [97, 96] revealed that a change in EEG activity of the cortex and subcortical structures occurred under the influence of much weaker current when the emotiogenic centers of the hypothalamus were stimulated than the current that induced arterial hypertension. It is apparent that emotional excitation, originally appearing in the hypothalamus and spreading in ascending and descending directions, is the prime factor in formation of hypertensive states.

The cited data from the literature are indicative of the important role of central mechanisms in onset of emotional stress states. Emotional excitation arising in the central nervous system when "conflict situations" persist for a long time changes into the "static form." Expressly this form presents the greatest danger, due to the continuous tonic influences of the constantly excited emotiogenic centers on the corresponding peripheral organs. Consequently, the study of central mechanisms of formation of "static" negative emotions constitutes a particularly important task for neurophysiology and theoretical medicine. First of all, one should devote attention to the study of cortico-subcortical correlations, investigation of the nervous substrate of emotional excitation of a negative nature.

The Nervous Substrate of Emotions

The aggregate of brain structures involved in formation of negative emotional stress includes, in addition to the hypothalamus, reticular formation of the stem, structures of the limbic system, various regions of the cerebral cortex.

The so-called emotional ring of Papez [151] refers to a number of structures of the limbic system: hippocampus, fornix, mammillary body, anterior thalamic nuclei and cingulate gyrus. The cingulate gyrus is viewed as the receptive area of emotions arising as a result of impulses from the hypothalamus. The hypothesis of Papez of continuous circulation of excitation within the limbic structures serves as a solid foundation for current conceptions of the mechanism of emotions; however, this scheme is not without flaws. Papez did not explain how emotional excitation is formed, what the role of the neocortex is in this mechanism, since without it there cannot be a conscious emotional sensation.

There is complex systemic organization of the mechanism of emotional excitation and its structural bases. Although formation of emotions is related to specific structures [20, 21], they are the result of activity of an integrated dynamic system that involves, if not the entire brain, at least different levels thereof.

Experiments of recent years have demonstrated convincingly how important the role of functional state of neocortical regions is in formation of a specific emotional set in animals. The studies of N. Yu. Belenkov [20] demonstrated that

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functional exclusion of the anterior segments of the cerebral cortex, including sensorimotor zones, increases general emotional tonus. Consequently, the emotional state of an organism is determined by the neocortex, which guides and forms the effector elements of emotions, making it possible for them to be of an adaptive significance. The temporal region of the cerebral cortex, which is directly involved in processes of afferent synthesis, fixation and reproduction of an animal's prior experience, plays a special role in forming the specifics of guided emotional states.

As we know, emotional stress states can be induced experimentally, for example, by the uncertainty of a situation when conditioned stimuli are associated, with some degree of probability, with delivery of electric current. In such an experimental situation, animals presented profound autonomic and endocrine changes associated with extremely marked behavioral reactions.

It should be noted that with all the seeming completeness of aggressive-defense reactions, they are quite different in decorticated and intact animals. The main point is that these reactions lose their adaptive meaning, direction, biological benefit in decorticated animals, and they arise readily in response to inadequate stimuli.

A. I. Shumilina [112] established that afferent synthesis of afferentations differing in meaning breaks down in lobectomized animals, with impaired evaluation of conformity of parameters of real results of action to the model formed as an "acceptor of action." These and other facts [113, 114] confirmed the conception of P. K. Anokhin concerning the predominant link between afferent synthesis and the "action acceptor" system and functions of the anterior regions of the cerebral cortex.

Differentiation of functions of the nonspecific subcortical system is achieved largely as a result of inhibitory and alleviating corticofugal influences.

In addition, it is known that removal of the entire neocortex from cats, with preservation of limbic structures, rendered the animals overtly apathetic and emotionally areactive [124]. However, it is remarkable that, as a result of such an operation, in response to exogenous stimuli the animals did not present the "false rage" reaction. All this led the authors to assume that not only the cerebral cortex but the limbic paleocortex have a restraining influence on the lower centers of the stem that determine aggressive reactions.

Some authors [128, 123] attribute the leading role in appearance of negative emotions to thalamic structures, stimulation of which in birds [23] leads to specific emotional movements. Destruction of the cerebral cortex does not eliminate this phenomenon.

Stimulation of the medial thalamic nucleus of man elicits the emotion of anger [133], which attenuates when the dorsomedial thalamus is destroyed. However, there are also other data on this score. Thus, emotions of fear and rage elicited by electric stimulation of several thalamic nuclei are inhibited by stimulation of the centromedial thalamic nucleus. In this case, the aftereffect of these reactions is briefer. Some authors [42] observed an attack reaction in animals as a result of stimulating their medial thalamic nuclei. Destruction of the dorso-

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medial nuclei intensified the rage reaction of cats. Thus, thalamic structures may have both an inhibitory and activating effect on reactions of a negative nature.

Some authors [124] established that emotional reactions are observed in cats even after resection of part of the olfactory brain, particularly the amygdala and medial cortex. At the same time, it was demonstrated that resection of only the cerebral cortex leads, on the contrary, to development of submissiveness in the animals.

Destruction of the amygdaloid nucleus in cats elicited the "false rage" reaction, whereas bilateral destruction of the structure of Papez' "emotional ring"--the temporal lobes, paleocortex, including the amygdala, entorhinal cortex, ventral hippocampus, as well as thalamic nuclei--led monkeys to an unusually calm state [137, 143]. According to other data, with simultaneous stimulation of the hypothalamus and amygdaloid region, the amygdaloid nucleus sometimes inhibited the attack reaction induced by stimulation of the hypothalamus [28, 53]. Interestingly enough, build up of fear and aggression, as well as attenuation of these reactions after removal of the amygdala, were observed by the same authors [108].

Disappearance of aggressive reactions of animals after resection of the amygdala and, on the contrary, appearance thereof warrant the belief that the amygdaloid nucleus has both an alleviating and inhibitory effect on lower mechanisms of aggressive behavior [124].

Thus, removal of the amygdala has different effects on manifestation of defense reactions. Perhaps this is related to extensive damage to this region, as well as distinctions of other structures of the central nervous system, with which the amygdala is closely linked.

It is known that the calm state caused by removal of the amygdala is followed by heightened rage after additional damage to the ventromedial hypothalamic nuclei.

When limited parts of the ventromedial hypothalamic nucleus are destroyed or removed, tame animals change to wild ones with vivid aggressive reactions that can be readily induced by even insignificant stimuli.

According to the hypothalamic theory of origin of emotions, the "central motivated state is maintained by stimulation of special hypothalamic centers which are influenced by the cerebral cortex, inhibitory hypothalamic centers and various humoral factors" [158].

The violent rage reaction to mild stimuli is manifested by animals both after resection of the cerebral cortex and destruction of the amygdala, ventromedial hypothalamic nuclei and even some thalamic nuclei.

Thus, these data are indicative of the existence of certain mechanisms that inhibit emotional reactions not only on the level of the cortex, but limbic structures of the brain.

As far back as the start of the 20th century, Sherrington [156] demonstrated that brief attack reactions, strictly related to stimuli, are observed in decerebrated animals. Manifestations of "false rage" persisted in animals after resection of all structures situated lateral, rostral and dorsal to the posterior hypothalamus and disappeared only after removal of this part of the brain [123]. Strong, overtly

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nociceptive stimuli are needed to elicit emotional reactions in decerebrated animals, whereas weaker, tactile ones are needed for decorticated animals.

On the basis of the experimental data, many researchers have concluded that the hypothalamus plays the initiating role in onset and formation of emotions and motivational states [94, 134, 97, 115].

In the 1960's, there was broad recognition of an analogous theory of Gellhorn [34] in which onset of emotions is also related to the hypothalamic system, with its rich bilateral connections to many structures of the central nervous system. In the presence of negative emotional states there is disruption of hypothalamic equilibrium, particularly between the anterior and posterior hypothalamus. In turn, these changes alter the intensity of hypothalamocortical correlations and are instrumental in formation of negative emotional and behavioral reactions. Gellhorn indicates that the limbic system plays the role of a sort of mediator between the hypothalamus and cerebral cortex, determining the quality of emotional sensations on the level of the cerebral cortex.

According to clinical data, the most marked mental disorders are observed when there are lesions to the posterior hypothalamus.

More recent studies revealed that the entire set of reactions characterized in intact animals by an affective state of fear and anger can be induced in mesencephalic animals. The reticular formation of the brain stem is particularly involved in expression of these reactions, which are the main signs of an emotional state [14, 19, 195].

According to the so-called activation theory of Lindsley [145], the leading role in onset of emotional states is attributed to the reticulohypothalamic system, excitability of which increases markedly with formation of emotions. This author discovered, in a study of EEG changes, that there was a decrease in activity of cortical regions and onset of "functional" decortication as a result of excessive stimulation of expressly that system.

As we know, the reticular formation of the brain has numerous anatomical and functional connections with various parts of the hypothalamus, thalamus, amygdala, as well as elements of the limbic system. Evidently, such broad relations of the reticular formation to other brain structures and, in particular, the cortex, upon which it has "specific" activating influences, determine its participation in forming emotional states.

Thus, extensive, functionally united parts of the brain are involved in forming emotional states: the hypothalamus, reticular formation, various limbic structures, as well as the cerebral cortex.

In addition, many researchers [133, 137, 98, 61] have indicated that there is functional dissimilarity of different structures involved in forming emotional tension of a negative nature. Analysis of these data requires that we dwell in somewhat greater detail on the complex diencephalomesencephalic part of the brain, hypothalamic centers and their correlations with other structures of the brain.

In the course of formation of integral behavioral reactions associated with emotional excitation, the hypothalamic "centers" interact with numerous other structures,

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forming certain functional systems, among which hypothalamo-cortical relations occupy a central place [46].

Removal of the cerebral cortex deprives emotional and behavioral reactions of their purposefulness.

The posterior hypothalamus has the most marked activating effect on the cerebral cortex, although there is also information about the corticopetal influences of its rostral parts [100, 150].

As for the anterior and lateral regions of the hypothalamus, they have an inhibitory effect on the cortex as a result of the depressing effect on structures of the activating reticular formation [132]. Thus, in general the hypothalamus has a tonic effect on the cortex: it stimulates, inhibits, regulates the level of brain activity and autonomic functions of the organism. Excitation arising in the hypothalamus determines the nature of the biological quality of various activations ascending to the cortex, lending a specific flavor to behavioral reactions and their emotional coloration.

The ascending influence of the hypothalamus on the cortex is formed in close functional interaction with the reticular formation, thalamus, amygdala and others. Many authors stress the functional unity of this complex [145, 150, 151].

By virtue of existence of the reticulo-cortical, as well as hypothalamo-reticular systems, the functional influence of the hypothalamus on the cerebral cortex is often implemented with the participation of the reticular formation.

On the basis of experimental data, K. V. Sudakov [97] established that it is expressly on the limbico-hypothalamo-reticular level, as a result of prolonged negative emotional states, that "static excitation" develops, which is the constant source of descending pressor influences on peripheral organs.

The reticular formation of the brain stem is important in this respect. Simultaneous stimulation of the reticular formation and posterior hypothalamus prolongs significantly EEG activation of cortico-subcortical structures and peripheral reactions. Anodal blocking of the region of the reticular formation of the mesencephalon, on the contrary, attenuates significantly the hypothalamic hypertensive reaction.

Thus, the main routes of dissemination of hypothalamic influences on the cerebral cortex may be either direct or through adjacent subcortical elements (thalamus, reticular formation, amygdala, etc.).

The existence of such diverse relations of the hypothalamus creates vast opportunities for its participation in forming the most complex reactions of the organism, including emotional stress that requires integration of virtually all of the main levels of the brain, including the neocortex.

Electroencephalographic Parameters of Emotional Reactions

One of the most widespread methods of studying electrical activity of the cortex and subcortical structures of the brain is electroencephalography [8, 89, 95].

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Numerous studies [1, 19, 64] pursued in the laboratory of P. K. Anokhin revealed that synchronized electrical oscillations at a frequency of 4-7 Hz, or so-called theta waves (Figure 2), arise in various cortical and subcortical structures of the brain in biologically adverse or "conflict" situations associated with negative emotional states. Participation of the adrenergic substrate of the reticular formation and hypothalamus in generating an orderly rhythm of 4-7 Hz (Figure 2) enabled P. K. Anokhin and A. I. Shumilina to consider this the "tension rhythm" or "stress rhythm," i.e., the electrographic expression of biologically negative emotional reactions.

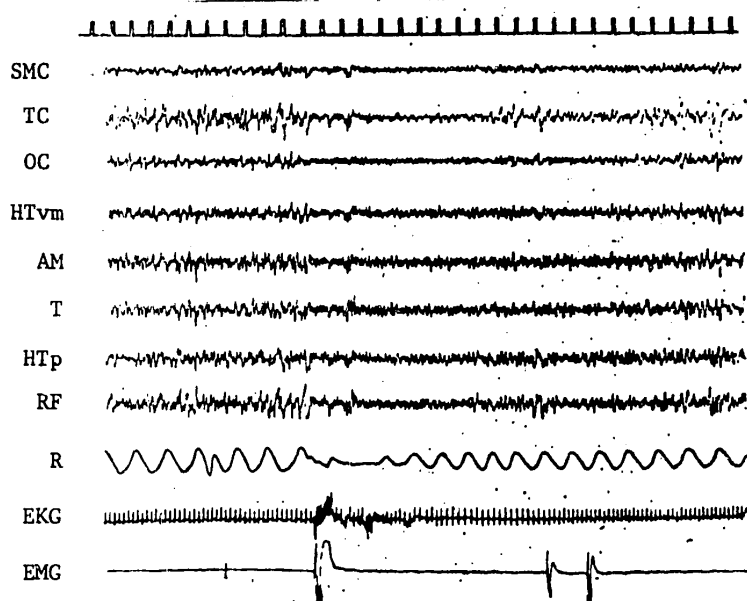


Figure 2. EEG of the cortex and subcortical structures of the brain

SMC) sensorimotor cortex	HTp) posterior hypothalamus
TC) temporal cortex	RF) reticular formation
OC) occipital cortex	R) respiration
HTvm) ventromedial hypothalamus	EKG) electrocardiogram
AM) amygdala	EMG) electromyogram
T) thalamus	

During development of a conditioned defense reaction to a bell combined with electrocutaneous stimulus, electrical activity at a frequency of 4-7 Hz was recorded in the reticular formation of the mesencephalon, thalamus, hippocampus, hypothalamus, as well as temporal and occipital regions of the neocortex, i.e., there was the same EEG change as with a nociceptive stimulus [111, 115].

Clinical observations of slow regular oscillations of electric potentials also confirmed the fact that an orderly rhythm of 4-7 Hz appears most often in the presence of negative emotional states--fear, pain, dissatisfaction [162].

Broad generalization over various subcortical and cortical structures of the brain is a typical distinction of tension rhythm.

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However, the expression of this rhythm is not the same in different structures of the brain. In the cortex, particularly the sensorimotor region, the 4-7 Hz rhythm is considerably lower in amplitude than in nonspecific subcortical structures. It has been established that EEG activity of the sensorimotor region is usually manifested in the form of a desynchronization reaction during formation of a negative emotional state of the organism; at this time, a distinct tension rhythm of 4-7 Hz is recorded from subcortical nonspecific structures [19]. With this, one observes changes in different directions in energy of the frequency spectrum of electrical activity of the cortex and some limbic structures [85, 66, 31].

In the neocortex, particularly its anterior regions, the energy of theta waves becomes lower than in subcortical structures where, on the contrary, it increases significantly.

Many nonspecific structures of the brain are involved in onset of tension rhythm. Destruction of various nuclei of the thalamus, hypothalamus and mesencephalon elicits disappearance of tension rhythm in all brain leads [141].

After bilateral electrolytic destruction of the posteromedial hypothalamus of mentally ill patients with marked aggressive behavior, the tension rhythm on the EEG changed to slow, high-amplitude irregular oscillations. Aggressive behavior disappeared and sleepiness appeared. The effects of such destruction persisted for 3 years.

Several authors [152] have called attention to the possible role of the anatomical system of the Naut (?) bond in appearance of theta rhythm. It is expressly the closed system over which there is continuous circulation of excitation that determines tonic activation of the cerebral cortex [10].

With repeated electrodermal stimulation, the intensity of EEG theta rhythm associated with autonomic changes depends largely on the stage of formation of emotional stress. Thus, at the first stage (1-1.5 h) this rhythm becomes dominant, whereas several hours later its amplitude increases significantly in the hypothalamus and reticular formation [97].

With continuous stimulation of negative emotiogenic centers of the hypothalamus for many hours, during the first hour a tension rhythm (6-7 Hz) is recorded in the reticular formation, amygdala, septum and hippocampus, which is associated with elevation of arterial pressure and change in other autonomic parameters. In the next 2-3 h of stimulation, these changes persisted. After normalization of somatic and autonomic parameters there was a corresponding change in EEG activity.

In the presence of negative emotional states, appearance of theta rhythm is governed by the law of probable reaction of the organism or information law of P. V. Simonov. This EEG parameter increases significantly in an uncertain experimental situation. In the course of developing a conditioned defense reaction, there is an increase in percentage of theta waves in the spectrum of the hippocampal EEG, which is associated with acceleration of heart rate. These changes are the most significant and stable under conditions of "pragmatic uncertainty" [86, 89].

A study of electrophysiological parameters of animals in situations differing in probability of "anticipation" of emotionally unpleasant stimuli confirmed the above-mentioned results (1). In these experiments, regularly timed electrodermal

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stimuli preceded by a flash of light were used, as well as random stimuli without the flash. For the first 3 h of the experiment, virtually the same stress states were observed in both situations. There was dominance mainly of tension rhythm on the EEG of the cortex and hypothalamus. The heart rate increased significantly. Motor reactions were the same, vocal ones appeared at the moment of electrodermal stimulation. After stimulation for 3 h there was a change in condition of animals in different groups. Thus, the heart rate and motor reactions diminished in the signal situation. Movements were made only in response to the stressor. In the intervals between signals the tension rhythm was replaced by high-amplitude but lower frequency oscillations. Tension rhythm was recorded on the EEG only during use of the stressor. In the "signal-free" situation, the changes in all parameters studied were persistent and more significant. At the same time, there were additional vocal reaction in periods between signals. The amplitude of tension rhythm increased by 1.5 times. In other words, in the case of "anticipation" of emotionally unpleasant stimuli there was less development of a stress state.

Impaired emotional activity elicits, first of all, disorders referable to cerebral processes characterizing the primary changes that arise at the very earliest stages of development of stress [95].

Changes in some parameters of cerebral homeostasis [33] make it possible to assess the functional changes in the central nervous system that are associated with corresponding changes in mental activity as well. The following EEG parameters were used to assess disturbances of cerebral homeostasis: overall change in EEG activity of the brain, stability of periods of alpha waves, etc. Impairment of cerebral homeostasis is manifested by drastic elevation, decline or fluctuation of level of excitability and lability of the central nervous system, inadequate replacement of one type of reaction with another, appearance of dissociation between components of the same reaction [40].

Many authors have observed a wide diversity of electrographic changes during formation of various emotional states in animals and man.

According to the data of some authors [145], depression of alpha waves and marked beta activity are typical of emotional tension in patients with neurosis and signs of emotional instability.

In addition, appearance of theta waves was noted with the use of tactile stimuli that are pleasant to animals. In the rabbit EEG, such activity was also recorded during self-stimulation, whereas stimulation of points that elicit a negative reaction was associated with desynchronization.

After creating chronic nociceptive foci in rabbits, some authors observed high-amplitude (up to 500 mV) and irregular slow (2-4 cycles/s) waves in electrical activity of the sensorimotor cortex, thalamus and reticular formation.

According to the data of N. P. Bekhtereva and V. M. Smirnov [25], the dynamics of slow EEG processes, in particular, changes in minute level of the constant potential in different parts of the brain, constitute a precise correlate of an emotional mental state.

The foregoing indicates that it is necessary to use more precise and objective methods of quantitative analysis for the study of the existing problem.

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This need is attributable to a significant extent to the fact that most authors assessed visually the EEG changes, which are quite complex and random. The need for strict mathematical analysis increases even more when studying the dynamics as related to exposure of the organism to numerous [or repeated] factors.

Mathematical Correlates

In the very earliest works of physiologists who studied complex electrical phenomena of the brain it became necessary to make an objective mathematical evaluation of its bioelectric potentials. The work of M. N. Livanov [59, 60] was a particular landmark in this direction.

At the present time, many researchers are using with success methods of quantitative processing of EEG's to study the functional state of the organism [49, 32, 63, 65, 74, 75, 117, 101b].

In the opinion of A. A. Genkin [36]: "Analysis of an EEG process could become considerably more effective if we were able to replace observation of the virtually boundless dynamics of a complex overall process with consideration of the dynamics of different parameters that would contain all or virtually all information about the general process."

For example, there is very precise correlation between a change in one of the parameters of electric potentials of the brain, phase asymmetry, ascending and descending fronts of EEG waves, and certain functional states of the body.

Reduction of phase asymmetry with repetition of "indifferent" stimuli in man was correlated in the same direction with the dynamics of autonomic parameters.

Changes in functional state of the brain and excitability of cortical neurons that affect the rate of formation of responses are closely correlated with changes in level of phase asymmetry: in the presence of mental tension this parameter rises and with fatigue it declines, and this is repeated in many experiments. One can assess the specifics of an activity--mental arithmetic, visual pictures, making a fist--from the nature of these changes [106, 35].

It should be noted that maximum changes in asymmetry of alpha wave phases in the frontal cortex occur upon stimulation of the thalamus, reticular formation and various afferent stimuli.

During the period of preparing for a voluntary movement, in the interval between warning and triggering signals, an "anticipation wave" is demonstrable in the anterior parts of the brain, manifested by an increase in positive shift of mean phase asymmetry of EEG waves. After a completed action and during repetition thereof this parameter declines.

The changes in this parameter become more static and stable in the presence of various brain lesions and psychopathological states [106].

A change in another time parameter of phase changes is also of some interest.

Analysis [84] of evoked potentials in the motor and occipital parts of the brain revealed that the phase shift observed between them occurs with the first presentations of light and disappears with repetition thereof. The phase shift

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increases again before appearance of conditioned reflex motor responses. It was found that the largest number of motor responses occurs in a specific phase of an evoked potential, when the phase shift reaches a maximum and comes close to its half cycle [period]. Consequently, there are phases of EEG potentials, in which there is alleviation of the motor response and phases of so-called relative motor rest.

Of special interest are sign-related phase shifts referable to slow EEG waves in the cortex related to emotional reactions. There is negativization of phases of these waves with positive emotions and positivization with negative ones [2].

Cross-correlation analysis revealed [43] that there is an increase in phase shift in the range of 4-7 oscillations/s between electric potentials of the motor and visual cortex in response to a conditioned defense stimulus. These changes were associated with an increase in cross-correlation coefficients and periodicity of theta rhythm. It cannot be ruled out, as believed by some authors, that the optimum conditions for dissemination of excitation among various regions corresponds to a phase shift other than nil. The authors made indirect evaluation of the magnitude of the phase shift (from the cross-spectrum), on the basis of the angle whose tangent equals the ratio of sine--transformation to cosine--transformation of cross-correlation function.

Of considerable interest is the study made by O. M. Grindel' of auto- and cross-correlation functions of the frequency spectrum of the EEG of the human cerebral cortex [38]. This author reports that the EEG waves in different ranges of rhythms are distinctly synphasic for symmetrical points of the occipital and frontal cortex. The coefficients of cross-correlation of electric potentials were higher in symmetrical leads than in frontal and occipital leads. Two forms of correlations were demonstrated in frontal-occipital leads: 1) cross-correlograms with prevalence of nonperiodic components and without phase shifts, indicative of the random nature of connection ("impulse connection") showing that there was simultaneous input of impulses from the subcortical region to both tested points of the cortex; 2) cross-correlograms of a periodic nature with phase shifts indicative of development of periodic processes in the two cortical points analyzed. The phase shifts were indicative of the order of dissemination of the process from one cortical point to the other.

The phase relations between the occipital and central regions of the human cortex depend on the nature of the EEG [38]. In the presence of alpha waves, the occipital cortex is ahead in phase and in the absence of these waves it is the central region. The phase correlations change under the influence of a photic stimulus, regardless of the nature of the EEG: the central cortex becomes the leading element, being associated with an increase in phase shifts (to 100 ms or more) and regularization of the EEG process [38]. In the opinion of the cited author, subcortical structures could be the initiating points that influence the cortex.

It was demonstrated with the use of a toposcope [152] that there is a 180° phase shift in synchronized theta rhythm between the cortex and diencephalic structures, whereas no such signs are noted between the hippocampus and diencephalon. EEG rhythms "shifted" at the rate of about 340 mm/s between different parts of the brain.

Cross-correlation analysis of phase shift of EEG rhythm (4-7 Hz) between the cortex and entorhinal ["entorial"?] region revealed [118] that, at the early stage of

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development of the conditioned response, the phase of subcortical theta rhythm was ahead of the cortical rhythms, whereas when the reaction was consolidated it was the entorhinal region, on the contrary, that was ahead (by 30-65 ms).

In the opinion of P. K. Anokhin, phase correlations, which are among the main parameters of reverberation processes, can serve as an indicator of activation of projection zones of the cortex and subcortical emotogenic structures during formation of emotional stress states. It should be noted that, according to a number of authors, various shifts of EEG wave phases modulate the level of excitability of brain structures involved in regulating the wakefulness level, memory processes and emotional reactions. For this reason, nonspecific [3, 24, 106] subcortical structures (hypothalamus, reticular formation) play the leading role in the genesis of slowly changing phase correlations associated with various metabolic changes.

The question arises as to how the changes in phase shifts of EEG potentials are related to "genuine" neurophysiological processes, upon which brain function is based.

The genesis of slow oscillations of phase correlations of EEG potentials, as well as changes in EEG waves themselves, are based on changes in synaptic and dendritic potentials [3, 106], since excitability of nerve tissue and metabolic tonus are determined not only by excitatory impulses traveling to neurons, but biologically active substances circulating in blood.

Some authors attribute the stability of changes in phase correlations of EEG potentials in different brain structures to changes in sensitivity of apical dendrites and postsynaptic slow potentials, as well as persistent biochemical changes in neurons [117, 126, 125]. Also, with regard to changes in phase shifts, importance is attributed to changes in neuronal cytoplasm, which occur under the influence of prolonged changes related to membrane polarization [159]. The increase in asymmetry of phases of the EEG process is interpreted as an indicator of prevalence of one type of polarization over others. These data are indicative of the electrotonic nature of phase correlations [35, 36].

Another statistical parameter--coefficient of cross-correlation--acquired broad use in studies of EEG potentials of the brain. The basic research conducted in the laboratory of M. N. Livanov revealed that there is more "alleviated" passage of excitation from the afferent system to the effector one with maximum values of the cross-correlation coefficient (Pax) than with low values. This thesis was demonstrated in a particularly distinct way in the works of V. D. Trush et al. [101], who compared excitability of the sensorimotor cortex with and without maximum correlation between cortical potentials. Excitability of the brain was determined according to the animal's motor reaction to cortical stimulation with threshold levels of electric current. The results revealed that, in the presence of maximum correlation of cortical potentials, mild direct stimulation of the sensorimotor cortex reached threshold values more often than without this maximum correlation.

The authors obtained analogous results in another way: they considered the ratio of dispersion of the electromyogram before and during stimulation. It was found that the mean magnitude of the reaction to stimuli delivered against the background of $P > Pax$ constituted 4.7, and with $P < Pax = 1.9$. Thus, in the presence of maximum correlation between potentials of the motor and visual cortex, the mean magnitude of the reaction (excitability) was considerably greater and the threshold of stimulation of the cortical region was lower than in the absence thereof.

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It should be noted that the fate of excitation spreading among cortical points may vary, depending not only on the values of the cross-correlation coefficients, dispersion of the EEG process, but phasic correlations between EEG waves (M. N. Livanov). This must be given a closer scrutiny. However, the mechanism causing "alleviated conduction" of excitation cannot be reduced to a change in excitability of only cortical regions.

Indeed, in 1967, I. N. Knipst demonstrated that, during development of the conditioned defense reaction, there was increase in synchronization of EEG potentials both in the cortex and subcortical structures (thalamus, hypothalamus, reticular formation of the mesencephalon). Depending on the stage of development of the conditioned defense reaction, he observed selective increase in synchronization of electric potentials of cortical representation of stimuli used and some subcortical structures. These changes were also associated with increased coherence in the theta rhythm range between cortical regions. After consolidation of the conditioned reflex, in the period between signals, both parameters again diminished. In contrast, the changes related to the direct effect of the conditioned signal were more persistent; however, when the reaction became extinct these changes reverted to the initial level.

It is believed by the authors that these changes reflect trace processes related to learning.

It is known that there is a drastic increase in number of highly correlated sections [60] in the cerebral cortex, particularly its anterior regions, during performance of mental work (problem solving). These properties of synchronization of electric potentials of cortical theta rhythms can be defined as processes that occur both in the cortex proper and subcortical structures. This was indicated by the decline of cross-correlation coefficients, which was demonstrated when the cortex was isolated from subcortical elements, during extinction of the conditioned defense reaction and after administration of pharmacological agents that block subcortical structures (sodium amytal, aminazin and others). Conversely, with electric stimulation of the posterior hypothalamus and reticular formation these parameters grew. M. N. Livanov relates these changes also to an additional 180° phase shift, which occurred as a result of prolonged "transfers" of EEG activity between the anterior and posterior cortical regions.

Thus, in the light of the data we have submitted, more comprehensive investigation of cortical-subcortical cross-correlations obtained from comparing electrical potentials of cortical regions directly to electrical potentials of subcortical structures acquires special importance.

I. N. Knipst demonstrated quite convincingly that, during development of the conditioned defense reflex, most leads with a high percentage of similarity of bioelectrical oscillations were referable to the cerebral cortex, somewhat fewer to subcortical structures (different parts of the diencephalon, reticular formation) and very few to cortical-subcortical parameters. These levels changed under the influence of stimuli, but the correlations between them remained the same.

It should be noted that concurrent investigation of phase correlations in these brain structures could perhaps disclose the reason why authors found different values for the cross-correlation coefficients.

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Much attention is also being given to analysis of coherence and dispersion [44, 43, 60, 101] to obtain a fuller idea about EEG processes. A coherence of close to 1 with a phase angle between two EEG processes in the cortex close to zero at a given frequency corresponds to a high positive correlation. Stabilization of the phase angle also affects this parameter. Special mathematical analysis revealed some correlation between changes in spatial synchronization of the EEG process, intensity or dispersion of a 4-7 Hz rhythm and their coherence. In particular, an absolutely objective pattern was discovered: low levels of spatial synchronization correspond to diminished coherence of the EEG processes analyzed or, as the authors explain it, presence of phase shifts between them.

Typical changes in spatial synchronization of EEG potentials within the cerebral cortex, which were demonstrated in the presence of certain pathological states of man, merit attention. Spatial synchronization was significantly greater in patients suffering from neurosis, schizophrenia and epilepsy, as compared to the norm. In the presence of neurotic states, the highly correlated segments were in the anterior and frontal regions, whereas in the presence of schizophrenia and epilepsy they were more often localized in the parietal and occipital regions.[60].

It is important to mention that, in the presence of neurotic states, changes in spatial synchronization occurred readily, not only due to conflicting words, but "indifferent" ones. But the main thing is that for a long period of time the same segments of the cortex consistently showed the same coefficients of correlation in neurotic patients, unlike schizophrenics and epileptics, which was indicative of persistence and stability of the correlations studied. The latter is particularly important if we consider that I. P. Pavlov considered that neurosis was based on signs of pathological stasis ["inertia"] and stability of impaired nervous processes. Thus, stabilization of expressly cross-correlations could be one of the indicators of formation of neurotic states.

Conversely, in the presence of schizophrenia and epilepsy, the cross-correlation coefficients are extremely unstable, not only in comparison to neurotic states, but the norm.

The authors arrive at the conclusion that, in addition to a cortical mechanism, subcortical structures are important to development of various pathological processes in the central nervous system, particularly the reticular formation and hypothalamus, the direct study of which in correlation with the cerebral cortex would enrich our knowledge about central mechanisms of formation of the static form of negative emotional excitation.

It should be noted that studies of the human cerebral cortex [38] in the presence of tumors of various cortical and subcortical structures revealed that they were associated with typical changes in cross-correlation parameters of the EEG. It was found that, in such cases, stable pathological "cyclic" correlations, with half-period phase shifts, appeared in the frontal and occipital regions. The change in direction of phase shifts, increase or decrease of cross-correlation coefficients and periodic components depended on the initial levels of these parameters and localization of the tumor. The most marked and persistent changes were noted with lesions to the anterior-frontal and diencephalic parts of the brain.

In addition to EEG studies, cross-correlation analysis is used with success in electromyography, as well as studies of electrical activity of sympathetic nerves of the heart, kidneys, etc.

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Chapter 2. Cortico-Subcortical Cross Correlation During Formation of Emotional Stress States

Some Distinctions of Cortico-Subcortical Cross Correlations

On the basis of conceptions [12, 94] of a "pacemaker" mechanism of formation of the main biological emotions and motivations, it was necessary, first of all, to determine whether distinctions of the pacemaker type of interaction between the analyzed brain structures affect the values of statistical parameters of electrical potentials of the brain.

With this in mind, studies were made of the correlation between slow EEG waves of cortical (sensorimotor, temporal and occipital cortex) and subcortical structures (posterior and ventromedial parts of the hypothalamus, reticular formation, amygdala, medial thalamic nucleus) with all sorts of variants of cross-correlation between them during and after delivery of electrodermal stimuli. The results of analysis of cross-correlograms revealed (Figure 3) that, in the vast majority of cases, slow waves of all analyzed structures were synphasic or, on the average, presented minor phase shifts (2.5-16 ms) before delivery of electrodermal stimuli. Only in the reticular formation did the changes sometimes reach 16-25 s. The strongest functional relations (up to 0.76) were noted between electrical activity of projection zones of the cortex (2) and their symmetrical parts (right and left hemispheres). They were somewhat lower (to 0.65) between subcortical (3) structures (thalamus, amygdala, ventromedial hypothalamus), and only mild functional links were noted between cortico-subcortical (4, 5) elements. However, the functional relationship was the most significant (0.75-0.8) between the reticular formation and posterior hypothalamus (1).

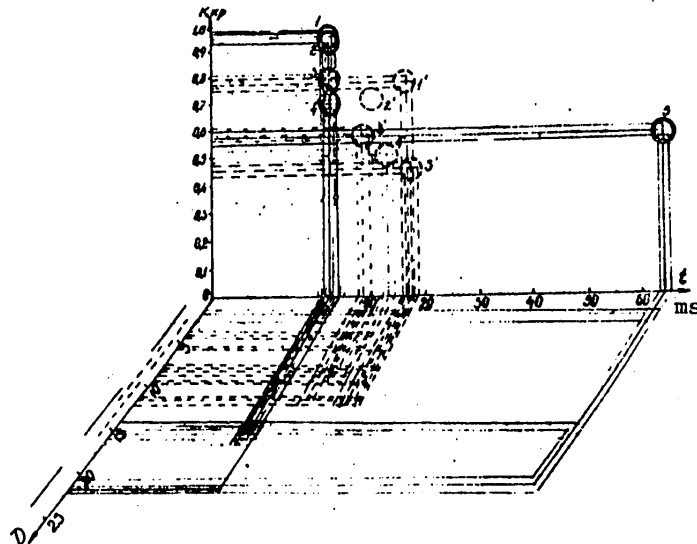


Figure 3. Distinctions of changes in averaged phase shifts (t , ms) of maximum cross-correlation functions (Kkp) and dispersion (D) of electric potentials of different structures of the brain. 1', 2', 3', 4', 5'--dash lines, background before electrodermal stimulation; 1, 2, 3, 4, 5--solid lines--after

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Cross-correlation analysis of slow EEG waves after electrocutaneous stimulation revealed an interesting pattern. The most significant phase shifts (up to the half period) appeared when we compared the slow EEG waves of the analyzed structures to slow waves of the posterior hypothalamus or reticular formation (5). These changes were indicative of phasic advance of slow EEG waves of the posterior hypothalamus and reticular formation in relation to slow waves of all analyzed brain structures, between which there were either insignificant phase shifts (2.5-16 ms) or none at all (Figure 3).

As for the functional relations, they were more accentuated after electrodermal stimulation; however, the ratio between different structures remained the same as in the background, before stimulation.

As can be seen in Figure 3, maximum increase of this parameter was observed among intercortical regions (2), and among the subcortical ones between the posterior hypothalamus and reticular formation (1).

As compared to these changes, the increase in functional relations of cortical regions to subcortical structures, particularly the posterior hypothalamus and reticular formation, was insignificant.

Maximum dispersion of EEG tension rhythm was observed in the posterior hypothalamus and reticular formation, somewhat less in other subcortical structures and least of all in the cortical regions of the hemispheres. Hence, maximum functional relations are demonstrable between electric potentials of structures, between which there are minimal phase shifts, associated with some difference in dispersion of electric potentials in each of the compared brain structures. With a greater difference in dispersion (Figure 3) and large phase shifts (to the half period) in electric potentials of compared brain structures, the functional relations most often are minimal. In other words, changes in maximum of the cross-correlation function in either direction are related to corresponding changes in phase shifts and dispersion of EEG tension rhythm.

Thus, the demonstrated distinctions of changes in cross-correlations between cortical and subcortical structures during defense reactions enable us to discuss the existence of "special" correlations of the posterior hypothalamus and reticular formations with various structures of the brain.

In addition, it is known that the hypothalamus, reticular formation of the brain stem, limbic structures, as well as the cerebral cortex, are directly involved in the physiological mechanisms of formation of an emotional state. However, expressly the hypothalamus has the exceptionally important capacity of transforming nervous influences into humoral ones and vice versa in the complex correlations between the cerebral cortex and subcortical structures. As a result, conditions are created for changing the needs of the organism into the appropriate and specific forms of behavior [94]. For this reason, when studying the dynamics of formation of emotional stress states, it is particularly important to detect the changes that occur in correlations between the hypothalamus and reticular formation, various elements of the limbic system, as well as projection zones of the cerebral cortex.

The program of correlation analysis of each experiment consisted of processing 10-s EEG segments, first in the background before use of stimuli. Then, similar 10-s EEG segments were studied in all experimental situations, during formation of

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emotional stress, just prior to use of stimuli, during delivery thereof and at different intervals between them: in the first half of the period closer to the end of electrodermal stimulation and in the second half, before it.

A state that develops in immobilized animals with the repeated use of stereotype or randomly timed electrodermal stimuli, which evoked drastic accentuation of inspiratory tonus of the respiratory center, twitching of the stimulated limb, occasionally vocal, as well as general motor reaction with attempts to get free, was used as a model of emotional stress. The emotional state that appeared under the influence of nociceptive stimuli is referable to the most primitive, "basic" (I. P. Pavlov) emotions of the defense type. Being one of the strongest ones, it elicits changes in all systems of the organism related to defense and adaptive reactions. It was borne in mind that, with the same physical parameters of stimuli, the degree of emotional tension depends on such purely information-related factors as stereotypy, randomness and signal value of the stimulus, i.e., those that mainly determine differences in possibility of "anticipating" emotionally unpleasant stimuli.

The 4-7 Hz (Figure 2) EEG rhythm that appears with negative emotional tension involves virtually all structures of the brain and, for this reason, is a good electrographic model for studying stressor states and their central neurophysiological mechanisms.

Correlation Parameters of EEG Potentials of Different Structures of the Brain in a "Signal-Free" Situation---"Randomness Factor"

According to biological theory of emotions [34], negative emotional tension occurs when feedback messages from the results of a performed action do not coincide with the previously prepared model of future events, the acceptor of action results. When there is prolonged imbalance, negative emotional tension increases and changes to a stationary form. For this reason, in the present series we selected the method of delivery of numerous irregularly timed (30 s to 3 min) electrocutaneous stimuli to the hind leg of an immobilized rabbit. Voltage was increased as the animals adapted to the nociceptive stimulus, starting at 10-20 V.

The conflict situation, in which immobilized rabbits received a painful shock [blow] and could not eliminate pain, was aggravated in this series by the fact that the animals were submitted to irregularly timed electrodermal stimuli, i.e., an uncertain situation, a so-called "signal-free" situation. Under the conditions of this experiment, this had the animals experiencing a constant negative emotional stress state, since with irregularly timed nociceptive stimuli there was a low probability (or utter impossibility) of their anticipating the time of delivery of emotionally unpleasant stimuli, and there was a severe shortage of "pragmatic information." Such information-related characteristics of the stress situation, which created difficult conditions, intensified negative emotional tension.

The data obtained on the first group of rabbits revealed that, before electrodermal stimulation, the slow oscillations of EEG potentials (Figure 2) of the sensorimotor, temporal and occipital cortex were essentially synphasic or presented minor (2.5-16 ms) phase shifts in relation to the posterior hypothalamus (Figure 4). The posterior hypothalamus was the advancing structure with regard to tension rhythm.

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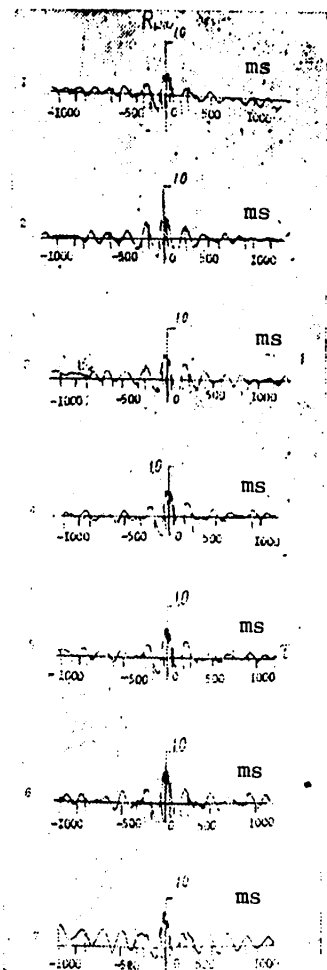


Figure 4.

Background cross correlations between posterior hypothalamus and various brain structures: sensorimotor (1), temporal (2) and occipital (3) cortex; ventromedial hypothalamus (4), amygdala (5), thalamus (6) and reticular formation (7)

It should be noted that the hypothalamic and cortical changes were the most significant in rabbits that presented synphasic relations between the hypothalamus and reticular formation even in the background, prior to electrodermal stimulation.

At the same time, there was a decrease in phasic changes of tension rhythm of the reticular formation and posterior hypothalamus in response to electrodermal

The functional associations, determined by maximums of cross-correlation functions with synphasic slow tension rhythm, between the hypothalamus and cortex were somewhat accentuated (0.45-0.6), whereas in the presence of phase shifts they were in the range of 0.4-0.5. Functional relations between the occipital region and hypothalamus were somewhat increased, as compared to other parts of the cortex.

Concurrently, half the rabbits presented synphasic slow, regular oscillations of electric potentials between the reticular formation and posterior hypothalamus, the maximum of cross-correlation functions constituting a mean of 0.75-0.85. The other half of the animals presented phasic changes (to 25 ms) between slow waves in these structures, indicative of a lag of tension rhythm of the posterior hypothalamus in relation to EEG potentials of the reticular formation. The maximum of the function between them was 0.7-0.78. The dispersion parameters, indicative of the energy of tension rhythm, were higher in subcortical structures (7-9) than in the cortex (6-7). Mathematical expectation or mean electric potentials of the analyzed structures were virtually in the same ranges--60.5-61.

Use of electrodermal stimuli against this background disrupted the synphasic conditions and elicited an increase in phase shifts in tension rhythm of all three projection zones of the cortex in relation to the electric potentials of the posterior hypothalamus. In other words, there was phasic advance of tension rhythm on the EEG of the posterior hypothalamus in relation to EEG activity of the sensorimotor, temporal and occipital cortex. There was elevation of maximums of cross-correlation functions, particularly in structures where they had been low previously.

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stimuli, which was associated with an increase in maximum of cross-correlation functions. When there were no phase shifts, the hypothalamo-reticular correlations remained synphasic even during electrodermal stimulation.

Repeated delivery of stimuli led to the following changes in the parameters we analyzed (Figure 5).

In response to electrodermal stimulation, phasic advance of tension rhythm of the posterior hypothalamus in relation to the rhythm of projection zones of the cortex and especially its sensorimotor region increased to a mean of 36-40 ms. All this was associated with an increase in maximums of cross-correlation functions (0.67), which were more marked when compared to slow waves of the sensorimotor region. At the same time the phase shifts between the posterior hypothalamus and reticular formation, on the contrary, diminished. Dispersion of tension rhythm increased in subcortical structures, whereas these changes were insignificant in the cortex. In the intervals between stimuli, we observed similar though somewhat less marked changes in maximum of cross-correlation functions, dispersion and periodicity of the process. Although the phase shifts increased, they were still less marked than during direct electrocutaneous stimulation.

By the 30th-45th stimuli, which were irregular, more significant changes were observed in the EEG parameters studied, not only during delivery thereof but in the intervals between them. These changes were recorded over the entire interval of EEG activity between nociceptive stimuli, which was indicative of formation of pretriggering integration. As in the case of direct nociceptive stimulation, these changes were manifested by more significant phase lags in slow waves of the tension rhythm of cortical regions, as compared to the posterior hypothalamus, reaching the half period or more (67-90 ms).

Dispersion of tension rhythm was substantially increased in subcortical structures (16-18), whereas in the cortex, on the contrary, it was decreased (4-5.5). While the major phase shifts were episodic at first, particularly in the background between delivery of electrodermal stimuli, after repeated use of stimuli these changes became increasingly stabilized. It should be stressed that the phase shifts were somewhat greater between EEG potentials of the posterior hypothalamus and sensorimotor cortex than in the relations between the hypothalamus, temporal and occipital regions.

After delivery of numerous irregular stimuli there were some distinctive features to the cortico-subcortical cross correlations, which consisted of a decrease in functional relations of the posterior hypothalamus with all cortical regions and, to a greater extent, the sensorimotor region (Figure 6). In 90% of the cases, the phase shifts were associated with a decline (0.15-0.3) of maximums of cross-correlation functions of the sensorimotor region and posterior hypothalamus. In the temporal region, the phase discrepancies were 10-25 ms shorter than in the sensorimotor cortex. In 82% of the cases, these changes were associated with a decline of maximum of the functions (0.2-0.3). Finally, considerable phase shifts in the occipital region, in relation to the posterior hypothalamus, occurred later than in the sensorimotor and temporal regions, and they were somewhat less marked. The maximums of cross-correlation functions declined (0.2-0.35) in 76% of the cases.

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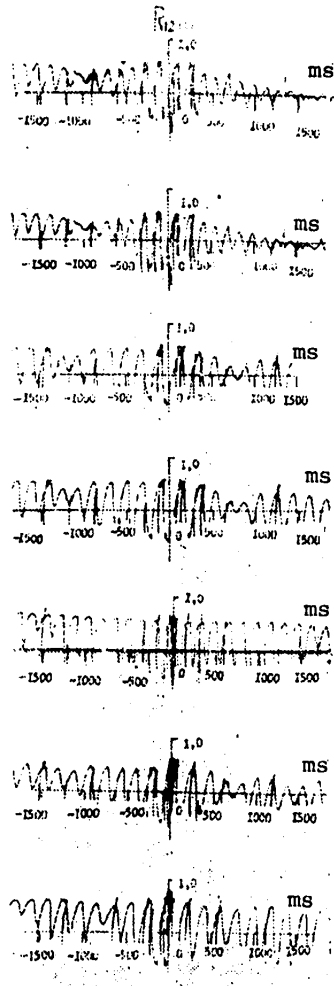


Figure 5.

Cross-correlograms of EEG tension rhythm after electrodermal stimulation.

Conventional designations are the same as in Figure 4.

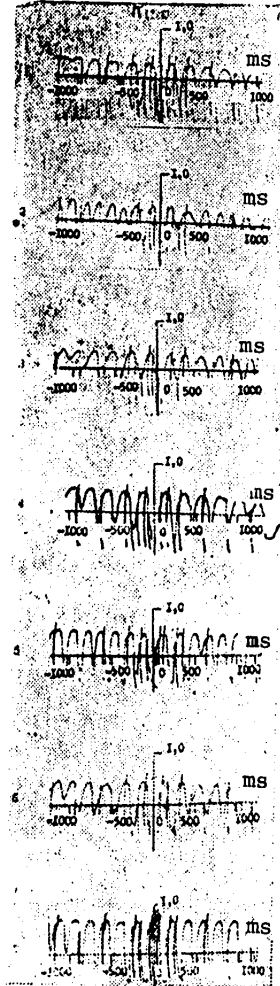


Figure 6.

Cross-correlograms of tension rhythm after delivery of numerous electrodermal stimuli.

The decline of cross-correlation function maximums was also associated with significant decrease in dispersion in the cortex, particularly its sensorimotor region. All this was indicative of the fact that multiple delivery of electrodermal stimuli led to a drastic decline in functional state of the cerebral cortex and attenuation of its relation to subcortical structures.

In contrast, closer functional relations were established between the reticular formation of the brain stem and posterior hypothalamus, which were manifested by completely synphasic low waves of tension rhythm, increase of maximums of cross-correlation functions almost to the limit (0.9-0.99) and increased dispersion in

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both subcortical structures to 15-25, which was indicative of increased excitability of these structures (Figure 6). The stable cortico-subcortical correlations established at this stage persisted in subsequent experiments (Figures 7, 9).

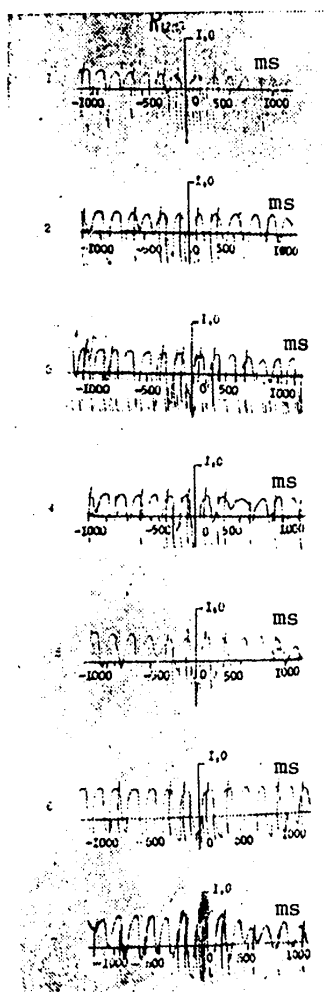


Figure 7.

19th experiment; stable persistence of cross correlations. Conventional designations are the same as in Figure 4.

hypothalamus- cortex and hypothalamus-reticular formation became very stable: no appreciable change to the end of the experiment in response to the stimuli or in the intervals between them, i.e., for 6-8 h (Figure 9). At this time, the coefficient of variation for the curves of distribution of maximums of cross-correlation functions was significantly lower than at the start of the experiment, which was indicative of stabilization of cross correlations. In the next

As for mathematical expectation of electric potential of the structures analyzed, the lack of change therein is one indication that there was no impairment of stability of the EEG during formation of emotional stress.

Expressly during this period, the changes in cross-correlation parameters of tension rhythm in the intervals between stimuli were the most significant and virtually the same as those demonstrated during delivery of the stimuli. It is important to note that these stable changes persisted continuously during the entire interval between stimuli. Vocal reactions appeared not only in response to the stimuli, but between delivery thereof. At this stage of emotional tension the rabbits presented dyspnea, up to 250 excursions of the chest and acceleration of cardiac activity to 300 beats/min (Figure 8). The animals became restless, aggressive, presented more frequent motor reactions manifested by twitching and even convulsive seizures, attempts to break away; some of them chewed through the wires; there were instances of aggression against the experimenter. Some animals urinated and defecated. After the experiments, there was heightened motor activity in the rabbits' behavior: as soon as the cage door was opened to give them water or food, the rabbits lunged and tipped the dish. This excited state was often associated with distinctive "growling." Some of these symptoms were associated in some animals with passive defense reactions of the "anxiety" [alarm] and "fear" type, while others were overtly in the nature of aggressive "rage."

After numerous stimuli, the changes in various directions referable to the

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experiments (starting with the second), such correlations were demonstrated in background EEG activity even prior to delivery of electrodermal stimuli, which was indicative of already formed pretriggering integration of the nociceptive emotional reaction. In view of the fact that stressor features in tension rhythm analogous to electrodermal stimuli were recorded also during the entire interval between stimuli and persisted in subsequent experiments, we can mention a rather important point: continuity of emotional tension in time during irregular delivery of stimuli, which is indicative of the animal's constant readiness for nociceptive stimuli (Figure 9).

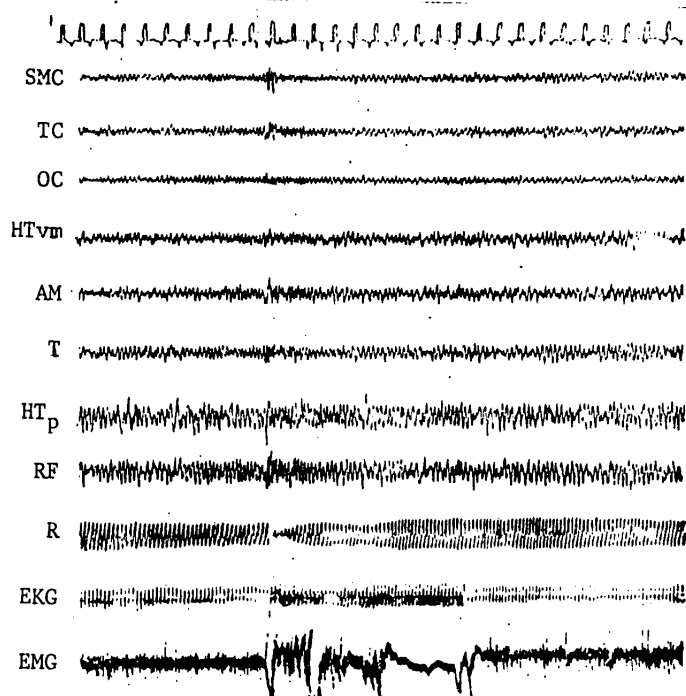


Figure 8. EEG, respiration (R), EKG and EMG following numerous deliveries or irregularly timed electrodermal stimuli [same key as Figure 2]

Delivery of numerous irregularly timed stimuli [68, 76, 147] caused a decline of cortical energy level and attenuation of its functional relations to the hypothalamic emotogenic zone, the excitability of which significantly increased (Figure 10).

According to the conceptions of I. P. Pavlov, a decline of cortical function and its functional relation to the "subcortex" could be indicative of development of "protective inhibition" in the higher parts of the brain when exposed to "excessive stimuli."

Analysis of changes in parameters of tension rhythm of the cerebral cortex, as related to the hypothalamus, revealed certain differences. Thus, EEG changes

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occurring between the posterior hypothalamus and sensorimotor projection region, where the most refined analysis of nociceptive stimuli is made, were the most significant.

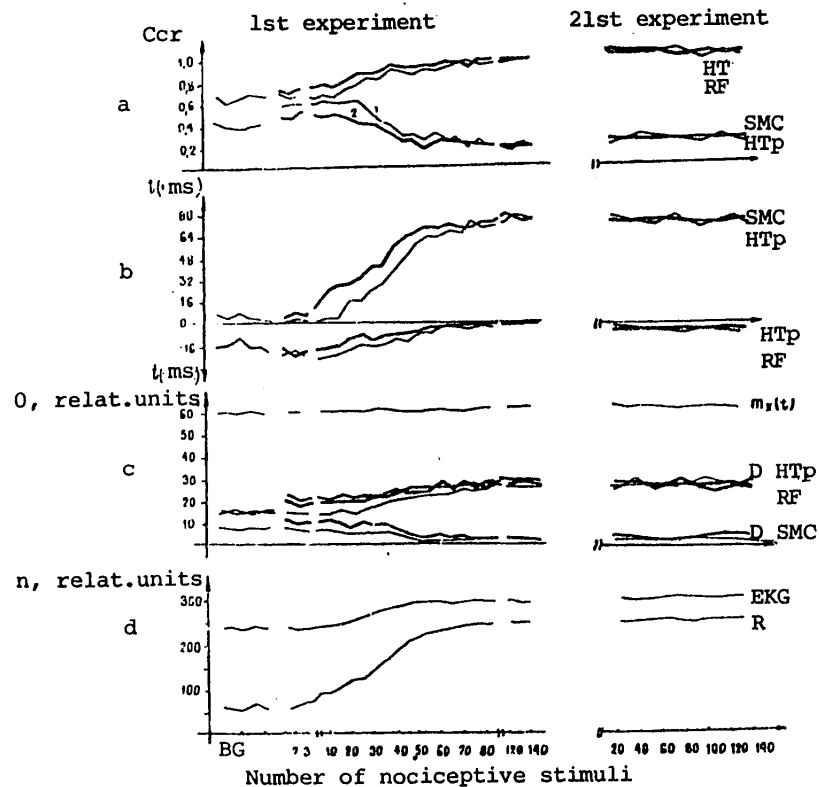


Figure 9. Graphic illustration of averaged hypothalamo-cortical (SMC-HTp [sensorimotor cortex--posterior hypothalamus] and hypothalamo-reticular (HTp-RF) cross correlations in first group of rabbits:
 1) interval between stimuli D) dispersion of tension rhythm
 2) during delivery of electrodermal stimuli n) heart rate (EKG) and
 BG) background respiratory excursions of
 $m_x t$) mathematical expectation the chest (R)

This means that, in stress situations, the anterior parts of the brain were the most sensitive, vulnerable, and this could, first of all, disrupt processes of afferent synthesis and affect making an adequate decision. Expressly these neocortical elements are essentially the acceptors of deep emotiogenic stimuli and participate in organization of complex forms of emotionally colored goal-oriented behavioral reactions.

The question arises as to whether the above-described changes in parameters of tension rhythm are limited solely to emotiogenic subcortical structures of nociceptive

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motivation and their projections in the cortex, or they also extend to interaction of the posterior hypothalamus with other subcortical structures of the brain also involved in forming negative emotional reactions. What distinctions are observed here?

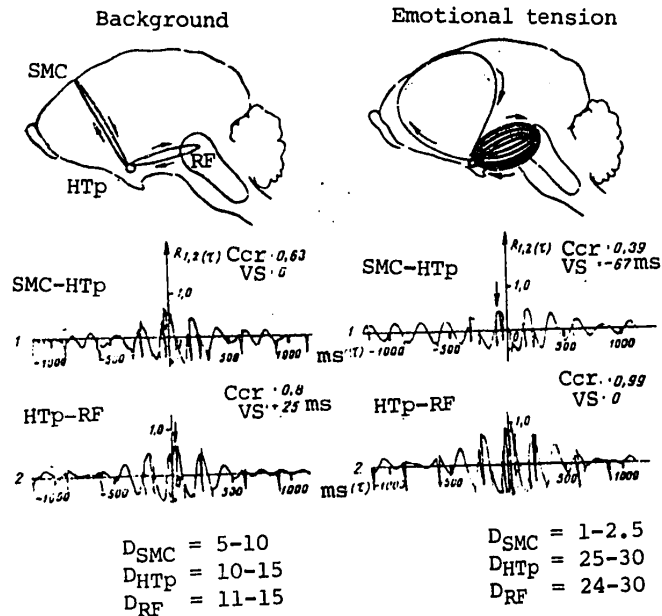


Figure 10. Schematic illustration of hypothalamo-cortical (1) and hypothalamo-reticular (2) changes in different directions

Key:

Ccr) coefficient of cross correlation [?"Kkr" in source] D) dispersion [?]

VS) expansion unknown

See Figure 2 for other abbreviations.

To answer this question, we submitted tension rhythm of the posterior hypothalamus in relation to slow EEG waves of the ventromedial hypothalamus, amygdala and thalamus during formation of nociceptive stress to statistical processing.

Analysis of cross-correlograms (Figure 4) revealed that the slow waves of the subcortical structures studied were essentially synphasic before delivery of electrodermal stimuli in relation to the posterior hypothalamus. The functional relations determined from the maximum of cross-correlation functions of slow waves of the posterior hypothalamus in relation to slow waves of subcortical structures were on the average in the range of 0.6-0.7; they were highest in relation to the medial thalamic nucleus and lowest to the ventromedial hypothalamic nucleus. The first deliveries of electrodermal stimuli to the posterior leg of the rabbit induced slight (16-25 ms) phase shifts in tension rhythm, mainly of the posterior and ventromedial hypothalamic nuclei and an increase in maximum of their cross-correlation functions. These changes were less marked than the cortico-hypothalamic parameters.

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After repeated electrodermal stimulation, the phase shifts between these structures increased to 67 ms and functional relations to 0.74 (Figure 5).

Thereafter, the phase shifts reached an average of 75 ms and became stabilized to the end of the experiment, but the maximums of cross-correlation functions dropped to 0.3-0.35 (Figure 6). As for the amygdala, the phase shifts of electric potentials did not change in relation to slow waves of the posterior hypothalamus. Of course, there were analogous findings in the intervals between stimuli. However, in this time, the other parameter of tension rhythm--maximum of cross-correlation functions between these structures--increased (0.76).

After 50-70 stimuli, the phase shifts of slow waves between the amygdala and posterior hypothalamus began to increase to 68-70 ms, and they were associated with decline of functional relations to 0.37-0.4.

Subsequent delivery of numerous irregular electrodermal stimuli elicited an increase in phase shifts between slow waves of the medial center of the thalamus and posterior hypothalamus. Concurrently, the maximum of cross-correlation functions between them dropped to 0.4-0.43. These relations between the posterior hypothalamus and analyzed subcortical structures became stabilized and persisted to the end of the experiment (Figures 6, 7).

It should be noted that dispersion of tension rhythm increased in all of these subcortical structures, but less than in the posterior hypothalamus and reticular formation.

In analyzing the physiological mechanisms of pretriggering integration, it should be noted that, as in the case of electrodermal stimuli, there were analogous changes over the entire interval between stimuli. This was indicative of the continuous nature of formed emotional tension with irregular stimuli.

Under these conditions, synphasic correlations and a high level of functional relations of EEG tension rhythm between the posterior hypothalamus and reticular formation were found to be the most stable (Figures 6, 7).

Thus, in the course of formation of nociceptive stress there were changes in correlations between pacemaker structures of nociceptive motivation and projection regions of the cortex, as well as various subcortical structures of the brain's limbic system.

The process advanced against the attenuated background of interaction of projection zones of the cerebral cortex with the posterior hypothalamus. There was an increase in phase discrepancies and decrease in functional relations of the ventromedial hypothalamus, amygdala and medial thalamic center with the posterior hypothalamus. Disruption of relations between subcortical structures intensified the state of tension. Indeed, we know from the literature that not only the cerebral cortex, but various subcortical structures of the limbic system can have a restraining effect on emotiogenic centers of the posterior hypothalamus and reticular formation.

We know [39] that reciprocal relations between electrical activity of anterior and posterior parts of the hypothalamus are disrupted under the influence of nociceptive stimuli. These changes alter hypothalamo-cortical correlations and cause formation of negative emotional states.

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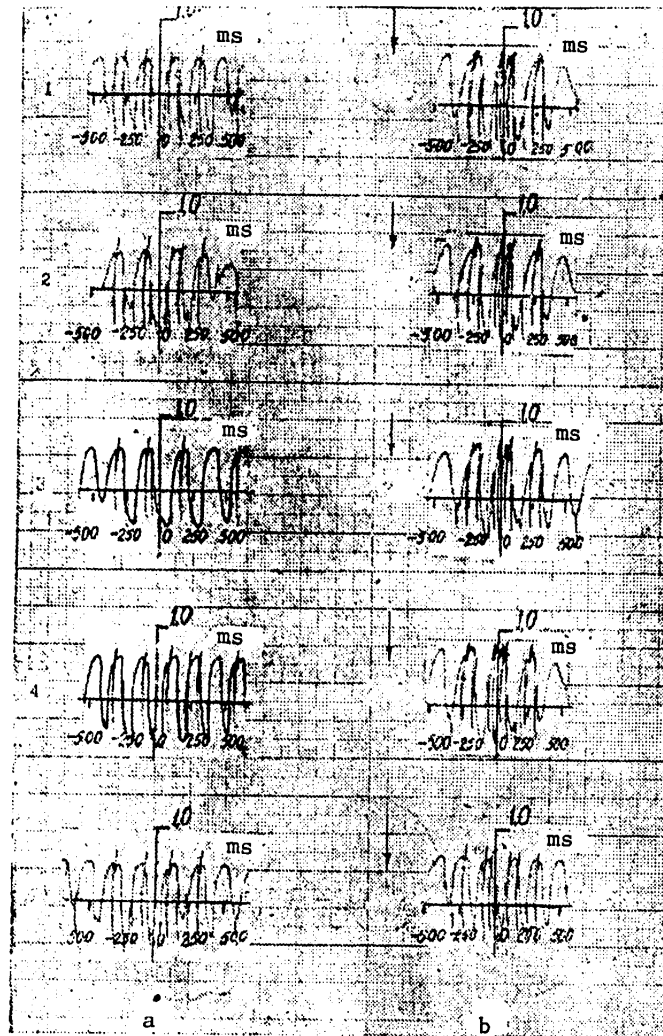


Figure 11. Cross-correlation shifts of slow EEG waves of the anterior hypothalamus in relation to electric potentials of analyzed brain structures: a) background; b) after electrodermal stimulation

It was demonstrated that there is a change in magnitude of phase shifts and maximums of cross-correlation functions between slow waves of the anterior and posterior hypothalamus under the influence of electrodermal stimuli.

The question arises as to whether these changes in parameters of tension rhythm are limited selectively to the system of the posterior hypothalamus and its projections in the cortex, or do they extend also to interaction between the anterior hypothalamus

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and the cortex and other subcortical structures of the brain. What distinctions are then observed?

Analysis of cross-correlograms revealed (Figure 11) that, before electrodermal stimulation, the slow waves of the anterior hypothalamus were generally in anti-phase (77-102 ms) with the analyzed brain structures, whereas maximums of cross-correlation functions were in the range of 0.4-0.66.

Use of electrodermal stimuli elicited changes in phase correlations, which began with a decrease in phase shifts between slow waves of the sensorimotor cortex and anterior hypothalamus. After 30-45 irregular stimuli, the slow potentials of these structures (1) became synphasic, while maximums of cross-correlation functions increased to 0.57-0.6.

After several exposures, a synphasic tension rhythm was also established between the ventromedial (2) and anterior hypothalamus. The level of functional relation rose to 0.6-0.67.

Continuing electrodermal stimulation elicited a decrease in phase shifts of slow rhythm of the amygdala (3) and anterior hypothalamus. The shifts in phases between the structures reached virtually zero values, and were associated with an increase of the maximums of cross-correlation functions to 0.56-0.7.

After delivery of numerous electrodermal stimuli, the same changes in phase shifts in relation to the anterior hypothalamus occurred in tension rhythm of the medial thalamic center (4). The maximum of cross-correlation functions rose to 0.65-0.72.

Numerous and irregular stimuli led to formation of the same changes in parameters of tension rhythm over the entire interval between these stimuli as during delivery of the stimuli. The altered correlations between the cortex and subcortical structures of the brain under the immediate effect of stimuli and in the interval between them, which became stabilized, persisted without noticeable changes to the end of the experiment.

Thus, we observed an inphase state between slow waves of the sensorimotor cortex, ventromedial nucleus of the hypothalamus, amygdala, medial thalamic center and anterior hypothalamus, which was recorded on a different phase level, shifted by a half period in relation to the slow waves of the posterior hypothalamus (Figure 11).

On the other hand, the shifts of slow waves of the same structures, in relation to the reticular formation and posterior hypothalamus increased to the half period or more, and were associated with decrease of functional relations. The phase shifts that were present prior to electrodermal stimulation between the anterior and posterior parts of the hypothalamus (99-102 ms) decreased to 65-75 ms at this stage of stress and were associated with an increase of functional relations to 0.5-0.68 (5). Perhaps, the functional "approximation" of these two parts of the hypothalamus was related to heightened excitability of its posterior part, which also "captured" other parts, including the anterior one.

The persistent changes in different directions in phase shifts and maximums of cross-correlation functions of tension rhythm of the cortex and subcortical structures indicate that, in the case of delivery of numerous irregular electrodermal stimuli, disruption of reciprocal relations is not limited only to the anterior

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and posterior hypothalamus. With regard to the latter, changes arise in different directions in parameters of tension rhythm of cortical and various subcortical structures of the brain. These changes are instrumental in forming stable negative emotional states. The posterior hypothalamus and reticular formation, the excitability of which increases significantly, play the leading role in generating tension rhythm.

Thus, functional relations and phase shifts characterizing the time and space correlations between the analyzed brain structures could be one of the indicators of organization of heterogeneous components of the functional defense system.

Electrographic Parameters of the Brain of Animals With Predisposition for
and Resistant to Emotional Stress

We discovered other patterns in the second group of animals, in addition to the submitted results referable to the analyzed statistical parameters of tension rhythm. They consisted of the fact that, after delivery of the first 2-5 electrodermal stimuli, there was significant increase in phase shifts (75-108) and maximums of cross-correlation functions (0.66-0.71) of hypothalamo-cortical correlations. These changes were observed both during delivery of stimuli and intervals between them. The new cortico-subcortical correlations were also associated with significant heterodirectional changes in dispersion of tension rhythm: increase in the posterior hypothalamus and decrease in the cortex. After delivery of 5-10 more stimuli the functional relations began to diminish (0.26-0.3) between the cortex and hypothalamus. At this time, similar changes also occurred in electric potentials of the posterior hypothalamus in relation to slow waves of the ventromedial nucleus, amygdala and thalamus. A complete coherence [synphasic state] and high relationship (0.95-0.99) were noted between the posterior hypothalamus and reticular formation. This persisted stably to the end of the experiment (Figure 12).

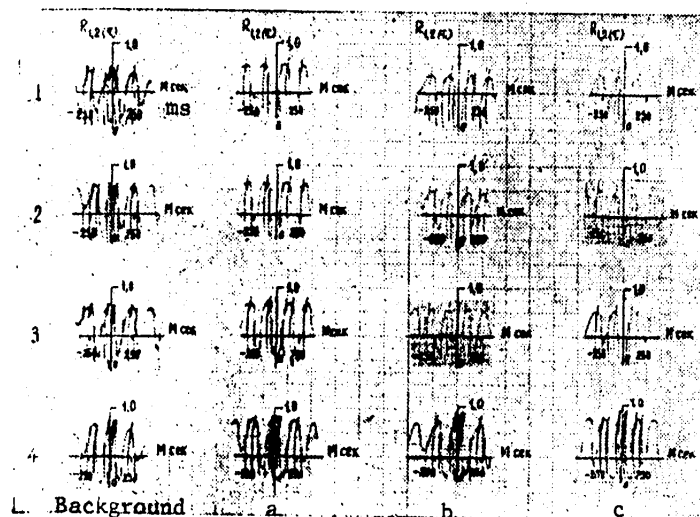


Figure 12. Cross-correlograms of tension rhythm obtained in second group of rabbits

a) after electrodermal stimuli

c) stabilization of cross-correlations

b) after delivery of numerous stimuli

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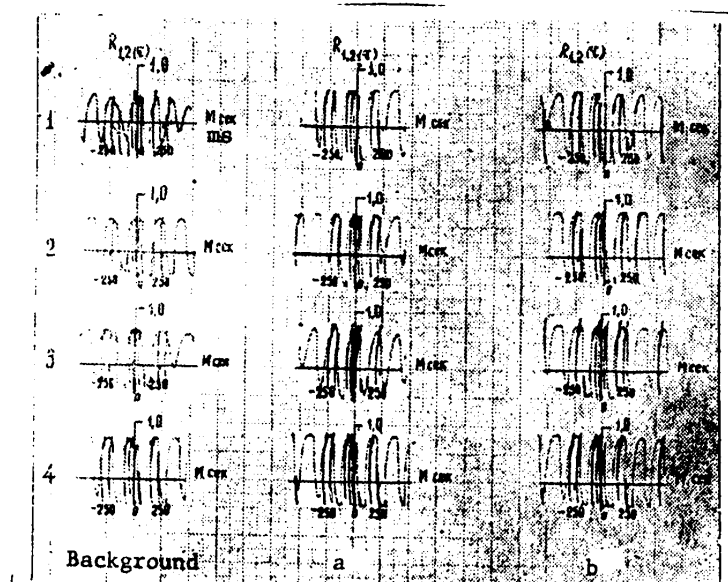


Figure 13. Cross-correlograms of tension rhythm obtained on third group
 a) after electrodermal stimulation b) after numerous stimuli

Thus, after delivery of several nociceptive stimuli, the second group of rabbits rapidly developed a stress state with the typical changes in statistical parameters of tension rhythm, autonomic components and behavioral reactions. Some rabbits of this same group presented faster pretriggering integration. We found that, in the first experiment, even before delivery of electrodermal stimuli, there were changes in analyzed parameters inherent in such states between the slow waves of cortical and subcortical structures.

Thus, the mere fact that these rabbits were immobilized constituted an effective psychoemotional stressor, eliciting the typical negative emotional reaction with all of the typical changes in correlation parameters of EEG potentials.

It should be noted that most rabbits in this group presented heightened excitability, even before the experiments were started. In their cage, the animals displayed typical avoidance reactions, receding into a corner. During immobilization, they were restless, escaped from being held in the hands and had vocal reactions; urination and appreciable dyspnea were often observed.

The submitted parameters characterizing individual distinctions of the second group of animals were apparently indicative of weaker resistance of their defense mechanisms to stress factors than in the first group of rabbits [71].

In addition, the hypothalamo-cortical phase shifts were slower and appeared only after delivery of 30-50 nociceptive stimuli in rabbits constituting the third group (Figure 13). In some animals, even after delivery of numerous stimuli in the first experiment, there was no impairment of coherence of EEG tension rhythm

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of the analyzed cortical and subcortical structures. This was associated with increase of maximum of cross-correlation functions (0.77).

It is only in the second experiment, in the same experimental situation, even prior to electrodermal stimulation or after delivery of several stimuli, that significant (60-70 ms) phase shifts appeared, which were associated with corresponding changes in autonomic and behavioral reactions. The conditions, under which the animal had first been submitted to numerous emotionally unpleasant stimuli, were rather potent factors capable of causing the entire set of changes in parameters that were typical of negative emotions. However, these changes were less marked in this group and they were associated with somewhat "diminished" hypothalamo-reticular functional relations (0.75-0.8) and partial coherence.

After delivery of numerous stimuli, the hypothalamo-cortical functional relations remained high--0.6-0.7 (Figure 13).

The changes in cortico-subcortical correlations related to individual distinctions of the third group of rabbits were indicative of greater resistance of their defense mechanisms to stressors than in animals of the first and second groups [71].

Cross-Correlograms of Electrical Potentials of the Brain During Delivery of Numerous 'Stereotypically Timed' Stimuli

The data obtained in the preceding series of experiments revealed that immobilized animals in a situation "without signals," submitted to numerous irregularly timed electric stimuli, experience constant and continuous tension, since they were unable to anticipate the time of delivery of emotionally unpleasant stimuli.

What changes will occur in the dynamics of formation of negative emotional excitation in the central nervous system when, under the very same experimental conditions, animals are submitted to regularly timed electrodermal stimuli, i.e., when the factor of chance is eliminated?

In this series of experiments, the effects of nociceptive stimuli were related to a constant time interval.

Delivery of numerous regularly timed electrodermal stimuli increased the probability of anticipating the moment of delivery of emotionally unpleasant stimuli.

P. K. Anokhin indicated that "when any criterion having a bearing on the organism is put in order, it already leads to organization of the system." As we know, I. P. Pavlov was the first to use the expression, "system," which was created during formation of the dynamic stereotype, i.e., in the case of delivery of the same stimuli in a recurrent order.

EEG studies revealed that, in the case of a fixed dynamic stereotype, for each forthcoming stimulus the brain automatically (on the basis of prior conditioning [or training]) prepares a state that qualitatively reflects expressly the stimulus that had been used many times in a given place.

Regularly timed electrodermal stimuli elicited the same typical changes in statistical parameters of the tension rhythm EEG as irregularly timed ones.

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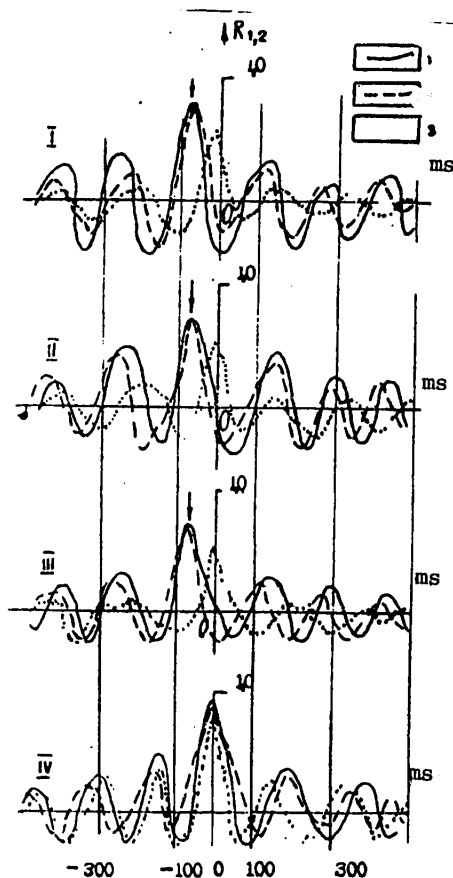


Figure 14. Cross-correlograms of tension rhythm after delivery of numerous regularly timed electrodermal stimuli

- | | |
|--|------------------------------|
| 1) immediate effect of stimulus | II) temporal cortex, HTp |
| 2) interval before delivery of stimulus | III) occipital cortex, HTp |
| 3) after delivery | IV) HTp, reticular formation |
| I) sensorimotor cortex, posterior hypothalamus [HTp] | |

However, in the case of delivery of numerous regular stimuli there were some distinctions pertaining to intervals between regular stimuli, i.e., pretriggering integration of the functional system (Figure 14). It should be noted that the direction of changes in cross-correlation parameters of tension rhythm in the intervals between stimuli was the same as during delivery of the electrodermal stimuli.

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Thus, after delivery of the first regular stimuli, the background EEG activity presented an increase in phase shifts, maximums of cross-correlation functions and periodicity of tension rhythm. These changes were equally demonstrable in both the first half of the interval, closer to the end of stimulation, and in the second half, just before delivery thereof. In other words, at first the formation of pre-triggering integration was the same over the entire interval between stimuli.

By the time stressors were delivered 30-50 times, the phase shifts and maximums of cross-correlation functions became more marked in the intervals between stimuli. However, in the first half of the interval between stimuli they were less marked than in the second half, just prior to delivery of pain. During this period, there was some differentiation of changes in pretriggering integration in different intervals: attenuation thereof in the first half and accentuation in the second, just before delivery of the stimulus (Figure 14).

From this time to the end of the experiment, maximum changes in cross-correlation parameters of tension rhythm in the intervals between electrodermal stimuli coincided with the time of delivery of the stimuli.

Thus, after delivery of numerous regular electrodermal stimuli, pretriggering integration, which includes the acceptor of action result, is not formed over the entire interval between signals, but is manifested in accordance with the law of dynamic stereotype, just prior to delivery of the electrodermal stimulus (Figure 14). There is final formation of pretriggering integration of the functional system, and it persisted not only to the end of the described experiment, but in subsequent ones.

As compared to experiments, in which irregularly timed electrodermal stimuli were delivered, in the above experiments there were less marked changes in autonomic and behavioral reactions. The rabbits were restless and aggressive, but to a considerably lesser degree. There were less frequent vocal reactions in the intervals between stimuli, and they occurred mainly just prior to delivery of a stimulus.

Comparative analysis of cross-correlation parameters of tension rhythms in the two series of experiments revealed that the typical changes in cortico-hypothalamic correlations were less marked with regular use of stressors than irregular use. And, while the situation of irregular delivery of the stressor "holds" pretriggering integration of the functional system in a state of "continuous tension," analysis of the EEG rhythm in the case of delivery of numerous regular stimuli revealed that its stressor characteristics appeared at a certain time, namely: exclusively at the time of delivery of the stimulus, and they were virtually restored to the background level after it (68). For this reason, in the case of regular stimuli, organization of the stress state occurs more slowly, with periods of decline of emotional excitation immediately after electrodermal stimulation.

Section II.

Chapter 1. Theory of Functional Systems--Cybernetics of Living Things

The conception of general theory of systems advanced in the early 1930's by L. Bertalanffy consisted of a general approach to large and complex systems of different types: engineering, socioeconomic and biological, including ecological communities [11, 102].

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Living organisms, as systems of a probabilistic nature, are notable for extreme complexity that is difficult to describe mathematically. The inherent distinction of such systems is that there are many interrelated variables that depend on numerous endogenous and exogenous factors.

P. K. Anokhin observed that the "exceptionally rapid growth in number of publications in the area of biological sciences, narrow specialization and appearance of new synthetic directions evokes a sense of helplessness in the face of the profusion of unsystematized information, and renders difficult collaboration between allied disciplines."

In this regard, the great physicist, Oppenheimer, stated in 1957 that "the more a researcher knows, the more he is aware of his ignorance" [50].

However, as far back as 1872, Claude Bernard observed that "the time will come when many specialists--philosophers, and poets, and physiologists--will speak the same language" [11].

At the present time, expressly systems analysis is the most constructive approach to synthetic problems of life, as it generalizes numerous and diverse analytical factors [10, 12].

Expressly general systems theory makes it possible to present the results of a refined analytical experiment in conformity to the specific patterns of the integral behavioral act and, as P. K. Anokhin says, "to span a conceptual bridge between these two approaches." Thus, it becomes possible to identify precisely the results of an analytical study of a large system.

It should be noted that the principle of "open reflex arc" of Descartes (1644), as it applies to living things, remained unchanged in the works of I. P. Pavlov, who discovered the conditioned reflex in the early 20th century.

In 1933, Academician P. K. Anokhin proved that there is a fourth element--feedback--which closed the arc. This is how theory of functional system of the organism emerged, which proved that its activities are based on self-regulation principles [7, 93]. P. K. Anokhin's functional system theory (Figure 1) views living organisms as self-regulating and dynamic systems, which have broad adaptation to changes in the environment. It is expressly through self-regulation of functional systems that there is manifestation of cybernetic patterns of life that are aimed at maintaining a positive adaptational result. Theory of information, control and feedback--the basis of cybernetics--can be applied with success to functional systems [93].

N. Wiener, the "father of cybernetics," related the prospects and main problems of biology expressly to self-organizing systems [30].

What is a system?

L. Bertalanffy [5, 51, 102] defined system "as any set of interacting elements"; others [11] observed that "system is everything that consists of interrelated parts." More recently [11], "the aggregate of elements related to performance of some function" is referable to systemic phenomena. However, such general definitions do not specify the real patterns of system function, since they apply to all phenomena in nature. The definition of system supplied by P. K. Anokhin is

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the most accurate. First of all, he observes that "if one accepts the definition of system as being only interaction of a set of elements, there would be unimaginable chaos in our brain that would not allow for any organized purposeful action." For example, the number of degrees of freedom of all neurons, i.e., all the possible interactions with one another, is so large that it would be hard to write down on a piece of tape 9,500,000 km long. For this reason, the entire question is to single out the factor that limits the number of degrees of freedom of aimlessly interacting elements in the system.

According to Anokhin, the useful end result is the factor that limits the degrees of freedom of various elements of a system (Figure 1).

A functional system does not consist simply of interacting components of the system, joined in a whole to obtain the useful end result for the organism [11].

"Functional system refers to dynamic organization of structures and processes in the organism which, independently of their anatomical and physiological classification, alter their architecture with exceptional flexibility in the search for a programmed result, which plays the part of a system-forming factor in selective mobilization of its different components" (P. K. Anokhin).

As we know, one of the distinctions of biocybernetic systems is their hierarchic structure, i.e., any system of a lower level is an element of a system of a higher level.

It is apparent that all of the lower level systems interact with one another and with a higher level system, being subordinate to the latter. It is important to note that this interaction occurs essentially according to the results obtained in each of the systems. This means that the hierarchy of systems changes into a hierarchy of results.

Theory of functional systems is a universal physiological model of the function of the organism.

Afferent synthesis is the initial stage of a functional system. At this stage, there is concurrent processing of information from triggering and situational afferentations, motivation and memory that dominate at a given time (Figure 1). Simultaneous processing of all four components is important, since it is only in such a case that each of them acquires the appropriate physiological characteristics. Expressly this property relieves the neuron from numerous degrees of freedom.

It is a known fact that many researchers are concerned with the time of fixation of information in the problem of memory. "This is unquestionably an important aspect; however, the center of events shifts from fixing to retrieval from memory of the information needed at a given time in the problem of setting a goal and decision making by the functional system" (P. K. Anokhin). In this case, we could be amazed at the ease and accuracy of such retrieval [11, 12].

It is very obvious that it is extremely pressing to study this mechanism of memory, and that it is impossible without simultaneous interaction of all four elements of afferent synthesis.

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This stage ends with setting the appropriate goal and making a decision for action (Figure 1). Let us mention that, unlike the most refined automated control systems, decision making occurs within the biosystem itself, not imposed from the outside. Making a decision relieves the organism of many degrees of freedom and forces it to effect only one form of behavior.

It must be stressed that the mechanisms of decision making are extremely complex and are still the most mysterious, and they must be worked on more effectively in the future. Thus, formulation of this problem ensues directly from theory of functional systems.

The value of a functional system lies not only in its methodological meaning, which relates the most refined analytical result to a large system, but in formulation of new research problems.

The system of action result acceptor is formed on the basis of afferent synthesis, after making a decision, concurrently with efferent messages in the brain (Figure 1).

In this anticipation system, the parameters of the model of the expected result are predicted in advance. Thus, real events are overtaken. The parameters of the results of a performed action are compared expressly to the parameters of this model by means of feedback. When the parameters coincide, a positive emotional state develops and the search stops (Figure 1). Noncoincidence of parameters is associated with a negative emotional state. A correction is made in the action through self-regulation mechanisms, and the search with the appropriate correction continues until the parameters coincide completely [93].

It should be noted that until the required positive result is obtained excitation reverberates in so-called "anticipation circles" of the acceptor of action results.

The parameters of the actually performed action are compared expressly to these "anticipation circles" by means of feedback. This is a manifestation of self-regulation of the functional system, which is a cyclic process aimed at regulating any parameter of the organism or maintaining it at a specific level.

Thus, anticipation of real events is of adaptive importance to living organisms. Let us cite a well-known example [54]. An animal having heard a danger signal becomes alert, but does not run even though its entire body is ready to run: the heart starts to function faster, respiration rate increases, the muscles are tense, etc. All of the complexes are directed toward assuring a positive adaptive result.

The most important distinction of the organism to anticipate the parameters of the result of an action not yet performed is used extensively in modern cybernetic machines. For example, the processes of rolling, aircraft flight are simulated on computers much faster than real processes. If the real processes do not coincide with preprogrammed ones, there is automatic readjustment of the control systems. Thus, like a living organism, the cybernetic machine [automaton] is able to anticipate [foresee].

Expressly the systems approach is the most effective in developing and using automated systems for analysis in the most refined analytical studies of complex physiological processes in the integral organism.

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Some Numerical Characteristics of Random EEG Processes

It is known that the EEG can be viewed as a sequence of locally stationary processes [57, 29]. This makes it possible to use, for analysis of the EEG, the correlation method that is one of the special cases of demonstration of nonrandom parameters of stochastic processes. The increasing use of this method to study complex EEG processes that have probabilistic-statistical organization [51] is attributable to the advantage of statistical analytical methods, accuracy and stability of the demonstrated parameters. The correlation function can be written down in the following form:

$$R_{xy}(\tau) = \lim_{T \rightarrow \infty} \frac{1}{T} \int_0^T [x(t) \cdot y(t + \tau)] dt.$$

Since we are dealing with finite processes, integration time (T) must also be finite:

$$R_{xy}(\tau) = \frac{1}{T} \int_0^T [x(t) \cdot y(t + \tau)] dt,$$

where $x(t)$, $y(t)$ are current values of functions, T is integration interval and τ is the shift in time of one process in relation to another.

1. With $x(t) = y(t)$ we have an autocorrelation function, i.e., the same signal is analyzed. The autocorrelogram enables us to characterize the mean frequency and degree of expression of dominant rhythm in one lead and does not contain phase information.
2. With $x(t) \neq y(t)$ we have a cross-correlation function, since $x(t)$ and $y(t)$ are different signals referable to different leads. Cross-correlation analysis determines the expression and frequency of the common periodic component of the two EEG processes examined. These components are singled out, even if their amplitude is considerably lower than that of random components. Cross-correlation analysis permits demonstration of the quantitative dimension of functional relationship of the two processes.

With a maximum relationship, this parameter tends toward one, whereas with statistically independent processes it tends toward zero.

3. Cross-correlation analysis makes it possible to determine the phase or time correlations between two analyzed processes according to the shift of maximum of the functions along the time axis. If there is no phase shift between two EEG processes, the correlation function is "even" [has parity?], and the function maximum is indicative of a zero shift, while other values thereof may either be the same or smaller [57, 29].

As we know, there is a relationship between the nature of the correlation function and internal structure of the random process corresponding to it. Depending on which frequencies and in which correlations prevail in the random function, the correlation function has one appearance or another.

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With $\tau = 0$, the autocorrelation function has a maximum value and numerically equals dispersion:

$$R_x(0) = D_x = \frac{\sum_{i=1}^n (x_i - m_x)^2}{n - 1},$$

where m_x is mathematical expectation, x_i is the value of a variable in the measurement and n is the number of measurements.

The overall EEG process can be submitted in the form of the sum of harmonic oscillations of different frequencies. The spectrum of the EEG process is a function that describes the distribution of energy [power] over different frequencies. Thus, the spectrum demonstrates the internal energetic structure of a given process.

The spectrum of a stationary random function shows the distribution of dispersion over different frequencies. Dispersion is the square of standard deviation of the random function from its mean value.

Spectral density $S(\omega)$, or energy spectrum of the process under study (distribution of dispersions over component frequencies), is the energy of the process averaged in time in the range of Δf frequencies.

$R_x(t)$ and $S_x(\omega)$ are closely interrelated and mathematically defined by one another using formulas of Fourier transformation:

$$R_x(t) = \int_0^{\infty} S_x(\omega) \cos \omega \tau d\omega$$

$$S_x(\omega) = \frac{2}{\pi} \int_0^{\infty} R_x(\tau) \cos \omega \tau d\tau.$$

In the case of analysis of the EEG, dispersion could serve as its precise amplitude characteristic for the segment studied [48].

Since a change in a stationary random function must proceed homogeneously in time, obviously the constancy of mathematical anticipation could be one of the indicators of stationariness of mathematical expectation:

$$m_x = \frac{\sum_{i=1}^n x_i}{n},$$

where x_i is the value of the variable and n is the number of measurements.

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Principles Involved in Construction of Equipment of Automated Systems
for Computer Processing of Physiological Data

In view of the fact that there is an increasing tendency toward moving from qualitative to quantitative descriptions in physiological research of complex, random processes, there is a greater need to refine methods of analyzing experimental data [18]. We refer, first of all, to the use of appropriate analytical methods by means of modern electronic computers. It becomes extremely important to use automated systems for processing physiological information. Automation of processing of the results of physiological experiments requires a set of equipment that transforms, gathers, stores and inputs biological information in computers [4].

Input of physiological data into a computer is done as follows: 1) conversion of analog information into a numerical code and input in the computer in the course of an experiment, i.e., in the "real time scale"; 2) digitizing biological data and punching them on papertape or recording them on magnetic tape with subsequent input in the computer.

Depending on the nature of experimental work and software used, either of the above variants may be given preference.

In the first variant, data processing on a computer in a "real time scale" makes it possible to conduct experiments that are controlled by feedback. In the second variant, in the course of gathering data it is also desirable to "control" the experiment, i.e., set the mode, duration and epoch of analysis, monitoring the conversion and recording of information, forming working codes and signals, etc. In the first variant, these functions can be assumed by the computer. In the second variant, where recording and processing of biological data are "spaced in time," it is desirable to use a device that must be able to control reproduction, starting, reading and inputting information in the computer.

A. The staff [4] of the institutes of cybernetics and physiology, Azerbaijan Academy of Sciences, under the leadership of Academician G. B. Abdullayev, corresponding member of the USSR Academy of Sciences, developed a special set of equipment to automate processing of physiological data on a computer (Figure 29), consisting of the following components: 1) multichannel analog-code converter designed to convert analog biological data into a digital code. Quantization in time and fixing analog values in all channels are done in parallel to eliminate the phase shift between input channels of the converter. Conversion into digital code and recording on tape are done successively. There is magnetic tape storage for recording and reproducing information that has been digitized and working codes (Figure 29 [not reproduced]). 2) The analog-digital recording device consists of a matching unit, analog code converter and perforator. In the analog code converter the following conversion principle is used: at each quantization step determination is made of the increments of input signal, which are stored in input recorders. For this reason, binary codes are formed in the output register after a certain number of quantization steps in time, from which one can determine, during computer processing, the numerical values of readings of the corresponding "segment" of the signal. The number of bit positions in the output register of the converter is taken as being equal to the number of tracks on the papertape. For this reason, one can record physiological information on series-produced perforators, the operating speed of which is 2-3 times slower than the frequency

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of conversion of input signals. 3) The programming device is intended to automate control of experiment mode and stimulation of the biological object, formation of signals at the start of conversion and zone number. This unit performs functions that provide for proper operation of the complex in the modes of retrieval and input in the computer of data from the magnetic recorder, as well as output of the perforator directly into the computer during the conversion process. 4) The unit that controls retrieval and input is designed to search for the zone number on magnetic tape, as well as tags indicating its beginning and end. In addition, it serves to receive digital and working [service] information, checking accuracy of its reading, packing [stacking?] and transmission to the computer. There are provisions in this device for linking it with different types of computers (Figure 29). 5) A unit that digitizes in conjunction with PL-80 or PL-150 perforators performs the same conversion also for punching on the papertape of multi-channel nonintersecting tracings recorded by electroencephalographs, analyzers and other instruments. The converters have been developed in two variants which use the effect of illumination of diagram tapes by a reader [read-out?] beam.

In the first variant, this is done by moving the infinite opaque tape with "reading slits," and in the second, by turning the opaque disc with transparent "reading slit." When light passes from the source through the mask slit, which is curvilinear, a "reading beam" is formed. During scanning, it moves over the trajectory set by the mask slit. At the moment the reading beam intersects the curve, the light guide with a photomultiplier turns dark and the value of the graph ordinates is fixed on the meter. The speed of conversion corresponds to the speed of the fastest modern keypunch machines.

Use of the above devices together with a computer increases significantly the operationality, precision and quality ["level"] of processing biological data.

B. The set of equipment [37] for processing physiological data on a computer, which was developed at the Institute of Normal Physiology imeni P. K. Anokhin, USSR Academy of Medical Sciences (Moscow) consists of instruments that are in the immediate vicinity of the biological object and in the central equipment (Figure 30).

Recording part of the complex: As can be seen in the flowchart (Figure 3), information from the object is fed into a 16-channel encephalogram of the Alvar Firm and from its amplifiers over communication lines to the central equipment commutation panel. Then the electric potentials are transmitted to direct current amplifiers of a type MN-7 analog computer for compensation of interference and amplification. Amplification is performed by means of 10 transfer [transient] amplifiers so that the output of the encephalograph (or frequency analyzer) matches the input of the "analog code" converter. Each transfer amplifier has three cascades with symmetrical output designed to alter the input signal in the range of ± 15 V. The frequency characteristics of the amplifier with disconnected load in the range of 0.1 to 50 Hz has nonuniformity not exceeding 3 dB.

EEG theta rhythm, singled out by the frequency analyzer, passes to the "analog code" converter for conversion of the analog signal into the pulse code required for input in the computer. Concurrently, there is production of working signals passing into the programmer. The "analog-code" converter has 10 input channels, and it is designed to code continuous signals from the transfer amplifiers in a

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"semizaryadnyy" [typo for 7-bit?] binary code. Each channel is "interrogated" at a frequency of 120 or 400 Hz. After the converter, the coded signals pass through the matching devices into the 16-channel magnetic type Astra recorder. The magnetic code recorder [pen] serves to record and store in coded form the signals coming from the "analog code" converter. Thus, the recorder serves as a buffer memory that permits "separation in time" of obtaining and processing information. The recording is made only at the intervals selected in advance. During recording, the data array is marked into zones by means of the generator that is started by the pulse-controlling programmer. A separate track on the magnetic tape is used for this purpose.

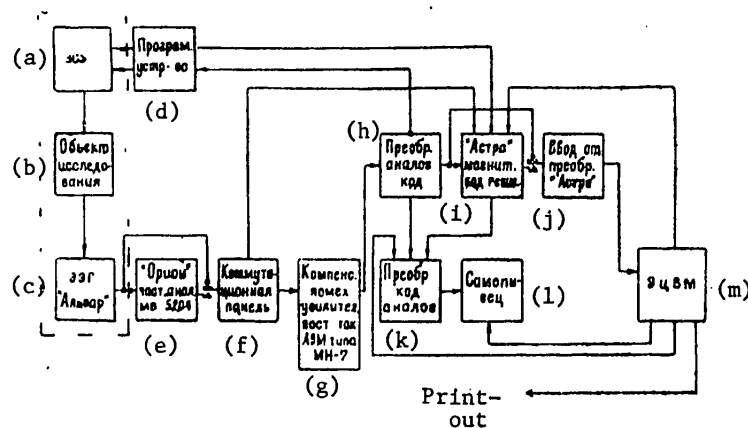


Figure 30. Flowchart of set of equipment for recording, converting and computer processing of electric potentials of the brain

Key:

- | | |
|---|--|
| a) ZSU [memory unit?] | h) analog code converter |
| b) object of investigation | i) Astra magnetic code recorder |
| c) Al'var EEG | j) input from Astra converter |
| d) programming unit 60 | k) code analog converter [conversion?] |
| e) Orion frequency analyzer | l) recorder |
| f) keyboard [commutation panel] | m) electronic digital computer |
| g) interference-compensating direct current amplifier of MN-7 analog computer | |

Operational part of complex: Two experimenters (physiologist and operator engineer) participate in each experiment, and they control the equipment. During the experiment, a stimulus is delivered to the object in the form of audio, photic or electric signals. The order of delivery of stimuli is specified in the program that is prepared before the start of the experiment. If necessary, the experimenters can alter the program of delivery of stimuli in the course of an experiment.

The programming device operation is based on choice of a specified impulse from a sequence and producing, in accordance with the time of selection, the controlling pulse signals specified in the program. In this case, the "cycle" signal from the "analog code" converter serves as such a sequence.

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The programming device has three independent channels. The signal from each channel is synchronized with either of the other two. Signals from these channels control external equipment. They consist of square-wave pulses of positive and negative polarity. In addition, the programming device has a unit for production of "loading" pulses (positive and negative polarity) the duration and recurrence frequency of which are altered by means of switches.

The beginning and end of generation of loading pulses are strictly synchronized with the leading and trailing edges of the controlling pulse by means of the cycle signal.

The "loading" pulses serve to synchronize the frequency and duration of stimuli. The program can be started by two methods, manually or from an external generator. The program is cleared either by the "reset" button or trailing edge of the controlling pulse. The data are recorded for 40 or 50 s, in accordance with the program. When processing on the computer, the zone marking makes it possible to input fragments of EEG information that correspond exactly to the time segments of the background, stimulus or aftereffect period.

Biosignals can be put into the computer from papertape, punchcards, as well as directly from the "analog code" converter or magnetic code recorder. The device for inputting data from the converter and magnetic recorder consists of a circuit for retrieval of a specific data array by the number of its zone and a circuit for channel selection for the purpose of selective input in the computer.

After processing on the computer, in addition to output on papertape and print-out, the data are transmitted to the "code analog" converter for conversion of binary numbers into their analog equivalent and simultaneous distribution in 10 channels.

The Question of 'Man-Machine' Systems

The set of equipment for automated processing of physiological data on a computer makes it possible to calculate the different parameters of complex EEG waves of the brain (Figure 29) quantitatively in accordance with the program.

In the case of preliminary recording of biological data on the magnetic recorder and subsequent processing on a computer, the processes of recording and processing are "expanded in time." In this relationship between the computer and brain, the latter is an object of effective investigation. After such quantitative analysis and "parametrization" of physiological functions, their "language" becomes "understandable" to the machine and the complex can be switched to the "real time scale" mode and mode of controlled experiments.

Demonstration of information processes of the brain on the "real time scale" opens up wide opportunities for studying brain activity.

If the codes of electric potentials of the brain corresponding to different events will be identified on a real time scale, with translation thereof into the precise language of feedback [opposites] in the environment, the specific electric activity of the brain will become a "model of behavior" that is accessible to investigation and practical application.

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The point of the above-mentioned experiments is that converted biological information is fed directly to a computer and, depending on the results of analysis, in the course of the experiment the appropriate opposite influence is exerted on any adjustable parameter.

In view of the relationship between the controlling action and result at the output of the system, one can calculate with precision the result of the action of various stimuli in order to alter the activity of the system in the required direction [50].

The principle of dynamic organization of complex biocybernetic systems with many feedbacks requires continuous multiparameter regulation, without which the system cannot exist.

The possibility of maintaining a specific state of the organism from the outside, with a computer, in the presence of variation of many variables, plays an important part in increasing the resistance of the system, which is instrumental in purposeful self-regulation [50, 54].

As can be seen in Figure 1, it is the most expedient to connect the automated system on the route of dissemination of the brain's commands to various peripheral organs or in the feedback circuit. Such a method of artificial self-regulation makes it possible to select the best mode for any functional system of the organism or, if necessary for research purposes, to "mismatch" the instructions issued by the brain and transmitted by the electronic device. Controlled experiments become particularly valuable in the study of self-regulating adaptive mechanisms of resistance of the organism to extreme factors and stress, as well as in the search for the means of influencing them effectively and selectively. In such controlled experiments, the organism is the object of effective influence on the part of the controlling computer.

The possibility of programming and mathematical formalization of physiological functions makes it possible to conduct a second type of controlled experiments with such a set of equipment, where the biological object itself--the brain--emerges as the main controlling element of the system. What is the main purpose of this aspect of research?

In the presence of intensive scientific and technological progress, there has been a drastic increase in requirements of automated systems of control of complex objects. However, one encounters major difficulties in this direction, which are related to the need to process an enormous amount of diverse information and organization of optimum consistency [matching] between man and a computer. In this respect, there is also the acute problem of developing the software to describe thinking processes and intelligence [16, 72].

For example, the difficulties involved in solving the most complex problems of national economic significance consist of the fact that, although the exact method of solving them is known--complete sorting of variants--this route leads to such enormous calculations that even a computer cannot handle them. As a problem grows more complicated the number of computer operations grow like an avalanche, which leads to processing of an enormous amount of information [54]. All this requires huge resources and time.

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Thus, if modern computers were to play a game of chess with complete sorting of 15-20 moves in advance, it would take them years. At the same time, a grand master of chess would need considerably less time and calculations for his next move [26, 103].

The human brain, being the optimum control system, has an entire set of indicators constituting its intelligence that enables it to solve the most complex problems the most efficiently with extremely little sorting. It is aided by the possibility of effective evaluation and screening of information by means of eliminating senseless actions, as well as the ability to formulate new tasks, problems and to use a creative approach to solving them [103].

Attempts to develop such technical systems with high ratings like living organisms are often limited by the capabilities of modern electronics, although some narrowly specialized machines could be superior to even man in some parameters (for example, speed and calculating capacity of computers, etc.). However, these are merely a few parameters of the millions that exist in brain activity. For this reason, when solving the traditional problem of a machine's ability to be "smarter" than man, one must compare the entire aggregate of parameters, rather than individual ones. In this respect, it is opportune to mention the graphic expression of P. K. Anokhin to the effect that a motorcycle could be "smarter" than man with respect to the one criterion of speed [43, 72].

In the opinion of P. K. Anokhin, "the ability to set a goal and make a decision, rapid change in various types of activity, as well as the presence of the system of emotions and intuition, extensive adaptive properties, anticipation of current events and flexibility, reliability and economy--is a far from complete list of indicators of superiority of the brain over the most sophisticated electronic control systems, including computers" [7, 43]. These distinctions of the human brain are related to the activity of billions of neurons and a fantastic number of correlations between them. There is not a single person whose memory is completely filled. However, A. M. Turing [54], the English mathematician, who expanded the theory of finiteness of the brain, believed that if one were to feed into a computer a prepared set of answers to all sorts of questions, the machine could replace human thinking. C. Shannon very validly objected: "According to Turing, there would be no differences between a person who solved a problem through thinking and an individual who memorized the solution in advance." Indeed, in Turing's model, the creative process, as one of the main indicators of human intelligence, does not exist.

It will be impossible to give a machine the above-listed qualities of the human brain and, in particular, emotions, intuition, genetic information, acquired life experience, self-awareness, etc., until thorough studies will have been made, primarily of their finest neurophysiological and neurochemical mechanisms. Moreover, algorithmization and development of the appropriate software to build models of these processes constitute one of the most difficult tasks for modern science. It should also be added that the International Conference on Artificial Intelligence (in Repino, 1978) arrived at the conclusion that "it is impossible at the present time using only numbers and calculations" on computers to force a machine to "think creatively," to create intelligence similar to man's in the complete sense of the word, "who not only can do everything but is also able to want to." For the time being, we could be dealing with enhancement of some functions of the brain and in rather limited areas at that--"chess computers," various dialogue systems and so-called "intellectual robots."

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However, at the present stage, the advances in robot construction are related primarily to devices that help relieve man of nonintellectual, heavy and monotonous work.

For example, manipulator arms, which do well on some lathes, scientific robots, the Lunokhod [LEM], etc., have gained fame in industry.

Another aspect of this problem has also gained a firm foothold. Nervous impulses of the brain intercepted on the way toward man's extremities help control powerful actuating servo-mechanisms that are used as artificial limbs, arms [manipulators] for handling reactive [nuclear] substances and thermal diving suits.[or space suits]. The reaction speed increases by a factor of 10. Man, so to speak, "completes" [builds on to] himself.

If we were to trace the trend of computer development from the first to the third generation, from lamp [tube] to semiconductor types based on integral circuits, multiprogram ones with universalization of language of communication with the operator, we would see that, although the process of development is directed toward the principles of function of the human brain, it is still very far from its capabilities. Suffice it to mention the huge problem of forming the purpose of control. A computer cannot set goals or make decisions. They are specified from the outside, by man, on the basis of his mind and motivation of behavior which are determined by exogenous and endogenous needs (Figure 1). Hence, the so-called "information hunger in cybernetics, due to the shortage of incoming information and intellectual hunger related to the limitations of a computer's black and white formalism" [26, 43]. "The computer, which made it possible in principle to relegate to a machine many aspects of brain activity, encountered some serious obstacles in creating artificial intelligence" [92].

For this reason, at the present stage, one should seek the solution to the problem of developing new, more sophisticated automated control systems for complex processes in the direction of using not only purely electronic systems, but combined neuro-electronic ones.

According to the conception of P. K. Anokhin, which discloses the main patterns of cybernetics of living things [93], all functions of the organism, from molecular to complex forms of behavior, are integrated into a whole on the basis of highly self-regulating functional systems (Figure 1), which is indicative of the effectiveness of creating combined neuro-electronic control systems.

More and more often, there is discussion in the press of questions of making practical use of combined biocontrolled systems [140].

A combined brain--rocket system is proposed in an article by Kelly [154]. After preliminary training of the cat's brain to identify a specific object, which arouses the animal's interest, it is connected into an electronic system. When, during an actual flight, the required goal appears on the screen, efferent nervous impulses will close the control triggering circuit. The instinct of a cat, which is such a remarkable mouser, helps it make a very accurate estimation of the jumping distance, speed of approximation and automatically react to evolution of the goal.

Such combinations simplify significantly the problem of pattern recognition and identification. However, development of combined systems has its own difficulties.

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Apparently, among the least difficult problems are those related to interaction between electronic systems and living cells, introduction of the transfer function of the living into the retrieval or guidance system. It is much more difficult to maintain viability of brain tissue when a living organism or part of it is used for a long time in the complex. Without this, the system immediately becomes inoperative [incapable of work].

Machines that are controlled by man constitute a special category of systems. The study of their properties, complexity of controlling modern machines and the need of optimum conformity thereof with the natural qualities of the human body is becoming an increasingly important task of our times.

Optimum distribution of functions among man and a computer increases the rating of the entire system. Such complex biocybernetic control systems consist of both living and nonliving elements [50].

Intensive research is being pursued in this direction: dialogue systems are being developed, which make it possible to communicate with a machine in the usual human language; systems are being developed for direct communication between the brain and a computer (the operator poses a mental question concerning course, speed, altitude of flight or means of solving more complex problems and the answer appears immediately on a "display").

Man of the future will, so to speak, link up with an electronic brain, and the closer such a brain will be to human intelligence, the stronger will be both the brain of man and of the entire system.

At an annual meeting (1977) of the Azerbaijan Academy of Sciences, Academician G. B. Abdullayev, president of the Azerbaijan Academy of Sciences, indicated that development of a solitary computer--brain combination at this stage would expand the capabilities of the computer with respect to making logical decisions based on abstract concepts, it would blend the high intuition and intelligence of the brain with its broad computing capacity.

G. B. Abdullayev made special mention of data [129, 138, 160] concerning a complex system of direct visually monitored control of action currents of the brain through the operation of a computer (Figure 31).

The demonstration unit consisted of a computer and "display" with a relatively simple maze marked on it, in the center of which a small mouse symbol moves (Figure 31).

Arrows were secured along the edges of the screen showing the direction of movement (up, down, to the right and left).

The subject participating in the experiment was situated in front of the television screen. Several sensors (5-6) were attached on his head which picked up weak electroencephalographic signals that were then amplified a million times and, after being converted into a discrete form, inputted in the computer. In the course of this experiment, while solving the problem of guiding the "little mouse" out of the maze, the subject looked closely at the arrow required at that particular time, which indicated the direction of movement. The computer, receiving the signals from the brain's action currents, processed them and issued the appropriate

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commands on the display, thus causing movement of the "little mouse" in the required direction. With proper decoding of impulses of the brain's action currents by the computer, 12 commands were sufficient to guide the "mouse" out of the maze, i.e., just as many as would be needed to perform this task by means of a control console.

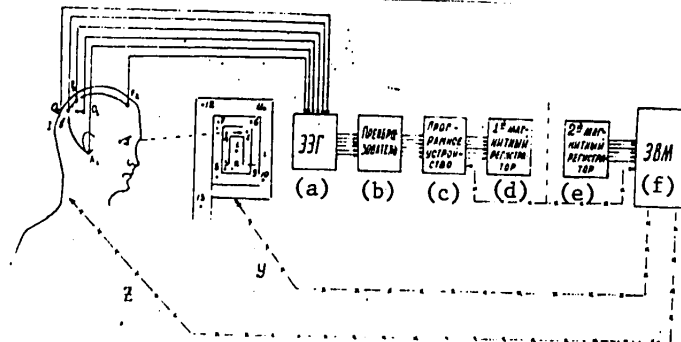


Figure 31. Visually monitored direct control of the brain's action currents by a computer

Key:

- 1-13) directions of movement of the "little mouse" on the display
- x) direct link to computer
- y) feedback with symbolic mouse
- z) feedback with human body
- I F₂, P₂, O₁, O₂) EEG lead from surface of cerebral cortex
- A₁) silent electrode

A total of 12 people participated in turn in controlling the computer in this manner. The computer underwent preliminary instruction about the "control style [handwriting]" of each subject, their complex controlling action currents. The mean level of proper classification of information on the computer constituted 90%, whereas a 99% level of precision is required for practical use of this method.

Work in this field is continuing, and the experiments that have been conducted enable us to outline the routes of future research.

This method of transmitting commands on a computer can be used, for example, to control machines and industrial processes, as well as in various emergency situations when it is necessary to turn something on or off rapidly. In practice, this means that upon detecting a deviation of any parameter of a unit that is controlled from the outside, it will be sufficient for a man to "issue a mental order" to change the parameters in the desired direction. In the future, such biological control will help develop a "routine" standard brain--computer linkage.

It must be noted that, for example, several tenths of a second are required to transmit control signals over radio, whereas less than 0.1 s is needed for direct control of brain action current impulses. To what can we attribute such a high speed of control?

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As we know, the human operator's transfer functions, which consist of transfer functions of the eye, ear, neuromuscular system (movements of the limbs, articulations, position), have a strong influence on the quality and effectiveness of control (speed, precision, reliability). Each transfer function introduces its own time lag or even "error" into the control system. For this reason, the most optimum conditions for control are to rule out intermediate transfer functions, i.e., to develop a system of direct control by a computer of the brain's action currents and the process [object].

For example, when an operator decides to depress some computer button, the impulses formulated in the brain extend over different levels, analyzer systems, through many cortico-subcortical pathways, pyramidal and reticulospinal tracts and effector organs.

Of course, this long and complex route traveled by a signal, which is picked up at the final stage of the functional system (Figure 1) takes much time. The probability of errors increases, and it is also closely related to the operator's psycho-emotional state.

The high speed of control when there is a direct link between the brain's action currents and a computer is achieved as a result of collecting information at the early stages of formation of functional systems (P. K. Anokhin), at the stages of afferent synthesis, or acceptor of result of action (Figure 1). This provides for a minimum number of transfer functions. In experiments of this type, it is quite sufficient to take information from the surface of the cerebral cortex. As we know, each complex function related to processes of thinking, learning and visually monitored reactions has its own cortical localization. Nevertheless, we should mention the important role in these processes of subcortical structures as well: reticular formation, superior colliculi of the lamina tecti [quadrigeminal plate] and others. The brief primary component of the evoked potential (EP) could serve as an electrographic parameter, which reflects arrival of information to the cerebral cortex. However, during processing, one must take into consideration more complex potentials that correspond to events (PCE). The PCE include sensory, motor, so-called "long-latent" potentials and artefacts. Detection and identification "on the real time scale" of these bioelectrical processes in the brain, which are related to various controlling commands of the biological object, require a special approach. Thus, although averaging methods have a number of advantages in detecting a weak signal in the presence of severe noise, there could be disappearance of the minutest EEG changes. For this reason, one uses identification of a signal for one run to identify the controlling commands of the brain on a "real time scale." This principle is the most effective, in spite of the fact that it is quite difficult to adhere to it because of the fine variability of PCE and effects of artefacts and instrument noises.

The software for processing action currents on a computer in the course of bio-controlled experiments is based on construction of a solving rule by means of heuristic programming. The processing scheme consists of a priori elimination of artefacts, use of Wienerian filtration, choice of tag vector, classification of epoch, as well as recursive elimination of ejects [138, 160].

It should be noted that rigidly determined programs cannot reproduce the higher logical functions of the brain and cannot take into consideration all of the unforeseen changes in complex, random action currents, which depend on numerous

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endogenous and exogenous factors. Loss of information increases even more when signals are classified for a set of subjects.

The probabilistic-statistical principle of organization of the brain enables it to find the most purposeful behavior in rapidly changing situations, on the basis of few base data, prior experience and intuition [72, 92], by the very shortest route, without examining senseless variants. This means that the ability to creatively solve the most complex problems with the least calculations is one of the main advantages of human intelligence over computers.

Thus, the brain has ways of reducing calculations, inherent only in it, and this is still among the unsolved mysteries of heuristics. Heuristic programs, which are used extensively in chess-playing computers, make it possible to depart from sorting to a significant extent and delineate the route over which one can achieve the most success. In assessing the chess position, the rules of the game are put into heuristic programs, which can subsequently alter the criteria for assessment and become improved [26, 72, 92]. The championships that have been held among chess computers revealed that the most promising programs were not the ones (of the "brute force" type), in which emphasis was laid on complete sorting of variants in the "truncated tree" of C. Shannon and speed of the computer, but those in which as many unnecessary moves as possible were eliminated from the "sorting tree," i.e., those that best approximated the way a chess master would play.

Thus, the greatest achievements are made with programs, in which there is less need to "calculate" and greater depth to the moves.

Heuristic programming of chess games on computers is very important to analysis and modeling of logical thinking, to future development of artificial intelligence and control of complicated industrial processes that require great calculations.

The so-called gyromatic programs of D. A. Pospelov and V. N. Pushkin, as compared to heuristic ones, are more based on theory of functional systems (P. K. Anokhin) and patterns of human thinking, which expands their capabilities significantly.

A gyromatic program forms the model of a future result, in which there is reflection of the gyromat and its correlation with the environment. Here, the obtained result is compared, by means of feedback, to the programmed model, while solving the problem with appropriate correction, like in the functional system, continues until there is total coincidence. In the opinion of its authors, the gyromat may even have a "consciousness" [26, 54].

Gyromats are multiprogrammed, they have a complex hierarchy and perfect themselves from problem to problem, so that one can solve on a more sophisticated level problems related to decision making [92].

It should be noted that both heuristic and gyromatic programs are merely special methods, which cannot totally replace human thinking. However, such simplified conceptions make it possible to "program" some narrowly specialized functions of the brain. Only broad use of theory of functional systems will help simulate in the future the entire aggregate of parameters of human intelligence and develop the most refined automated systems for the control of complex processes without the participation of man.

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Thus, development of new systems "encounters" a number of difficulties in different directions of science, which are related to the limited capabilities of modern electronics, computer software and the problem of artificial intelligence. However, at this stage, development of a solitary brain--computer complex with optimum conformity, which would combine the advantages of the living and electronic systems, would expedite the solution of complex control problems in many respects. Regardless of how effectively some direction or other will develop, the "systems approach" to the study of this problem is indisputable and, as a result, so is the mutual enrichment of neurophysiology, medicine and electronics.

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